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SURGERY, GYNECOLOGY AND OBSTETRICS

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A REVIEW CLINICAL AND PATHOLOGICAL OF PARAHYPOPHYSEAL LESIONS[1]

CHARLES H FRAZIER, M D , Sc D , F A C S , PHILADELPHIA PENNSYLVANIA

ONE has but to glance at the pages of the medical history of this country to realize that the name of Philadelphia is closely knit to medical tradition—the home of the first medical school, of the first hospital as well as clinical laboratory, of the first public health endowment to promote public health as a profession, of the first hospital clinic for teaching and of many other pioneer institutions The chapter of surgery would be far from complete without the name of William Shippen Jr , the special pupil of William Hunter, of Philip Syng Physick, called the father of American surgery, of William Gibson, of John Rhea Barton, of George McClellan, and George W Norris, ranked among the best surgical writers of his day, of Thomas Muetter, of Joseph Pancoast, of D Hayes Agnew, of Samuel D Gross, of W W Keen

Thomas Muetter, born in Virginia in 1811 graduate of the University of Pennsylvania, professor of surgery Jefferson Medical College celebrated for his plastic operations for extensive scars, died in 1859 May 1 of this year, the College of Physicians agreed to change its location to Thirteenth and Locust Streets and his widow offered to deposit his library and pathological museum with the College when a permanent building for its reception should be constructed Through this benefaction the Muetter Museum and the Muetter Lectureship were established

Since the inauguration of this foundation many deposits have been made in the Museum and 46 lectures have been delivered

In London on November 27 of the present year,[1] exercises were held to commemorate the Jubilee of the first operation for the removal of a tumor from the brain performed by Sir John Rickman Godlee, but we are inclined to associate the name of Sir Victor Horsley with the recognition of neurosurgery as a special field of surgical endeavor Since that time and more particularly since the beginning of this century, neurosurgery has been recognized as a special calling and for this credit must be ascribed to the United States Not for a long while, in fact not until recent years, did the countries across the Atlantic begin to train personnel for this specialty

The extraordinary advances in the surgery of brain tumors is a matter of common knowledge In 1894 at a meeting of the American Neurological Association one of its members reported a series of 3 cases of brain tumors treated by massive doses of potassium iodide and of this number 2 were alleged to be markedly improved What a transition from 1894 to 1934!

One could not begin to encompass now in a single treatise the problems of the surgery of brain tumor so diversified and so differentiated have they become no more than one could in one treatise the surgery of abdominal

[1] Muetter Lecture delivered under the auspices of the College of Physicians of Philadelphia December 6 1934

tumors. Since the notable contribution of Cajal to the differentiation of glial cells, one could not in a reasonable time comprehend the many questions that concern even a single type of tumor—the glioma.

In search for a subject appropriate for this Muetter Lecture the author has chosen to consider the problems of brain tumors from a regional viewpoint and will present a collective review of the lesions that may be styled parasellar Within the limitations of a space no greater in diameter than half a dollar one may find at operation any one of eight lesions —lesions that differ from one another in their source of origin, in their histological components, in their clinical behavior in their influence upon the expectation of life in their management on the operating table, to wit

I Intracranial aneurisms.
II Tumors of the optic chiasm
III Sphenoidal ridge tumors.
IV Pseudotumors.
V Rathke s cleft tumors
VI. Hypophyseal stalk tumors.
VII Suprasellar fibroblastomas.
VIII Suprasellar adenomas

GROUP I PARASELLAR ANEURISMS

When considering lesions in the parasellar area, one must bear in mind the possibility of aneurisms of the circle of Willis Those which arise from the internal carotid artery from the middle cerebral and the posterior communicating vessels, may properly be considered as in this territory As to the incidence of intracranial aneurisms Osler found 12 in 800 autopsies and Pitt 23 in 900 autopsies Of 154 assembled by Gowers, 23 arose from the internal carotid artery 44 from the middle cerebral and 8 from the posterior communicating artery Approximately half of the total number originated in the territory with which at present we are concerned

The cause of cerebral aneurisms is not clear Syphilis plays a very unimportant part even in young individuals. A congenital weakness of the vessels at the point of bifurcation with a defect in the muscularis has been advocated warmly and appears to have some basis in fact In older individuals, unquestionably arteriosclerosis is a factor Mycotic aneurisms when they occur are more common in the cerebral than in the basilar vessels. In the case I am about to cite the patient was in her twentieth year with no definite sclerosis of the vessels and it seems reasonable to assume that the aneurism was of congenital origin, that is, due to a congenital defect in the muscularis.

CASE 1 A month ago for a period of a week a young woman had attacks of nausea, vomiting, and headache with pain referred behind and over the right eye. A second attack followed with paralysis of the third and fourth cranial nerves While under observation she became comatose, developed a right hemiparesis, and died The autopsy revealed a ruptured aneurism of the posterior communicating artery probably congenital in origin.

Clinical history H M K aged 20 years, (File No 10645) was admitted to the Neurosurgical Service of the University Hospital August 8 1930 Briefly the history was as follows

June 29, 1930, the patient stepped into a swimming pool and suddenly developed a right sided headache Pain was referred chiefly over and behind the right eye She became nauseated and vomited but did not lose consciousness The nausea persisted for 2 days and the headache for 5 days She remained in bed week and returned to her occupation as a professional nurse in 3 weeks

August 1 1930, a month after the initial attack, she felt faint and vomited several times Headache was present but less severe than aforetime August 2 she developed an oculomotor palsy Her menstrual periods had been irregular for 4 months

August 1 1930, with the exception of paralysis of the third and fourth cranial nerves there were no neurological signs except a slight cut in the left temporal field (Fig 1) The serological reactions were negative and there was no blood in the cerebrospinal fluid

August 2 1930 she was found unconscious in the bathroom She remained comatose or semicomatose, developed right hemiparesis, and died August 27

Autopsy revealed a ruptured aneurism of the posterior communicating artery with hemorrhage 1 to the right ventricle a subarachnoid hemorrhage at the base and covering the entire right cerebral hemisphere The brain was markedly edematous The origin of the aneurism was obscure unless it was congenital According t Dr B J Alpers, there were changes in the carotid vessels which strongly suggested the chronic vascular syphilis of Jacob (Fig 2)

Upon reviewing this history one is impressed with certain features characteristic of aneurism and chiefly with the periods of active symptoms and remissions, associated with a sudden and otherwise unaccountable paralysis of the oculomotor nerve In this case the

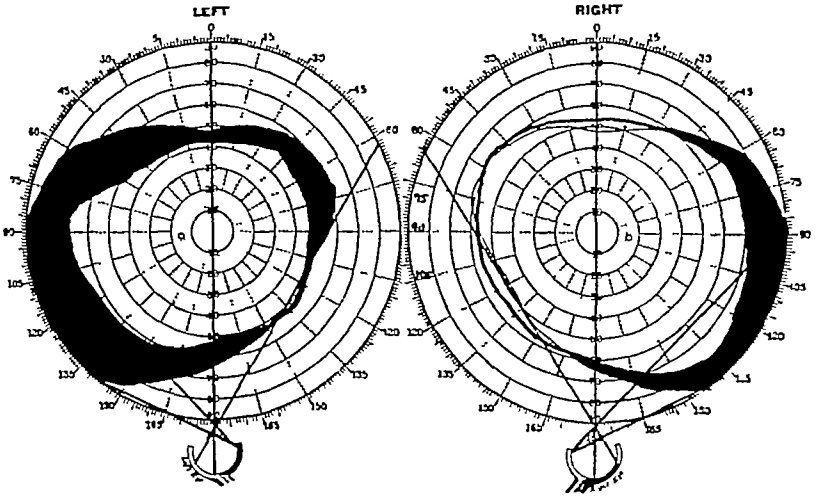

Fig 1 Case 1 Contraction field of left eye in an intracranial aneurism of the posterior communicating artery

interval of freedom was comparatively short, though in others months and years may elapse between the attacks

In addition to the oculomotor paralysis, the fourth cranial nerve and the ophthalmic division of the fifth were involved Furthermore the patient had had the intense headache that so frequently accompanies leakage It is not without reason to assume that the irregular menses were due to pressure on the hypophysis Among the ocular phenomena of parasellar aneurisms may be included field defects

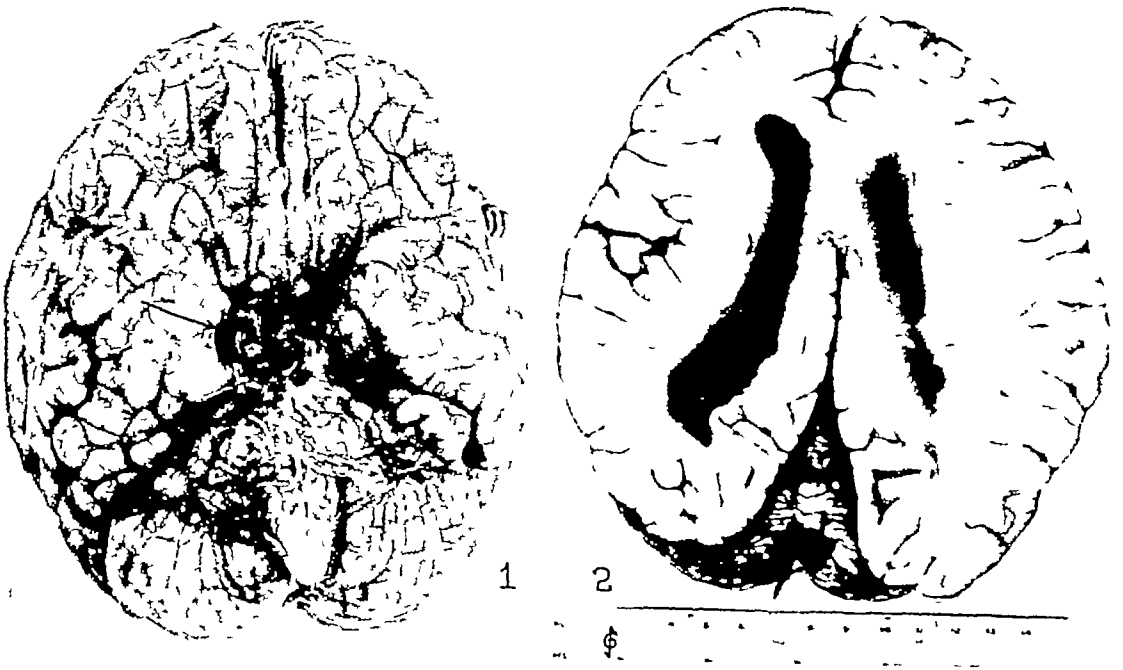

Fig 2 Case 1 Left, The arrow indicates a small aneurism arising from posterior communicating artery and compressing the oculomotor nerve Right, Section of brain showing intraventricular hemorrhage which caused death.

Fig 3 (Case) A large saccular aneurysm (A) on the left arising from the internal carotid and a smaller one (B) on the right arising from the same vessel

(as in this case) ptosis, strabismus diplopia, proptosis edema of the eyelid and venous engorgement from pressure on the cavernous sinus

The second case to which I will refer differs from the first in that there was definite evidence of arteriosclerosis of the circle of Willis and the patient was in his fifty-third year But there was in this case no oculomotor or other ocular palsy The outstanding symptom was an intense paroxysmal pain in the ophthalmic division of the trigeminus

(Case) A middle aged man 5 months before admission to the hospital in the course of 3 weeks had a series of attacks characterized by intense headache left frontal neuralgia and momentary unconsciousness Then followed a remission until 3 weeks before admission when he suffered intense paroxysmal pain in the distribution of the ophthalmic division of the trigeminus Under the assumption that he had trigeminal neuralgia he came to the Lenox Hospital and died two days forewarning 4 hours after admission Diagnosis large aneurism of the left and a small aneurism of the right internal carotid artery

(Case) R W M aged 53 years (File No 140937) was admitted to the Neurosurgical Service of the Lenox Hospital August 22 1932 Except for a latent tuberculosis, the patient was well until March 3 when he felt nauseated on arising and lost consciousness for a few moments These attacks of nausea and unconsciousness recurred several times a day for a week and were accompanied by an intense bifrontal headache and extreme tenderness of the left side of the forehead He complained at times of smelling a foul odor Meanwhile there were no visual disturbances Three weeks after the onset of these attacks the symptoms subsided, but 3 weeks ago he began to complain of shooting pains over the left eye, more or less paroxysmal The patient a physician, thought he had trigeminal neuralgia and decided to consult Dr Frazier His wife stated that he had become somewhat disorientated, had a poor memory for recent events, was emotionally unstable and increasingly irritable He was admitted to the Hospital at 6 45 p m and died suddenly 4 hours later

Examination At the preliminary examination it was noted that the pupils were small, equal, and reacted promptly to light and accommodation There were no ocular palsies and the fields were grossly normal The right tendon reflexes were hyperactive with an unsustained ankle clonus In other respect the examination was negative

Autopsy At the autopsy there was revealed a thick subarachnoid hemorrhage which extended from the basilar area to the lower end of the medulla An aneurism 2 5 by 3 centimeters in diameter was found in the left internal carotid artery just below its junction with the middle and inferior cerebral arteries The aneurism compressed the diencephalon and mesencephalon and extended laterally into the uncus and hippocampal gyrus of the left temporal lobe The left oculomotor and left optic nerves appeared compressed There was a small aneurism at the junction of the right internal carotid and middle cerebral artery There was definite arteriosclerosis of the circle of Willis (Fig 3)

In this as in the preceding case, despite the fact that there were no ocular palsies, there was the history of attacks, which suggested leakage followed by remissions In the case under consideration the attacks were characterized by intense headache and periods of momentary unconsciousness Intense headache rigidity of the neck ocular palsies, and a positive Kernig sign of sudden onset If not immediately fatal should always arouse one s suspicion of intracranial aneurism

Were one to consider differentiation from a parasellar tumor the gradual onset of the symptoms in tumors should at once eliminate the likelihood of an aneurism To be sure a parasellar tumor may cause pressure on the third fourth and fifth cranial nerves, often with field defects, but the patient never ex

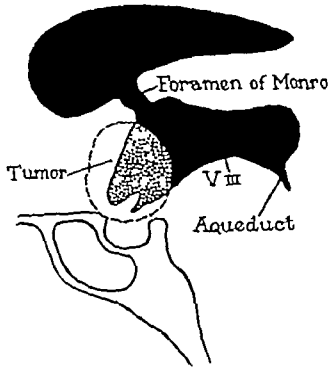

Fig 4 The deformity produced by gliomas of the optic chiasm as shown by lipiodol injection into the ventricles The anterior portion of the third ventricle and the infundibulum (dotted area) are obliterated by tumor The sella is normal

Fig 5 Case 3 Glioma of right optic nerve

hibits the signs of leakage or rupture, the intense headache and the stiff neck with blood in the cerebrospinal fluid Nor in the history of the tumor case are there striking periods of remission

GROUP II TUMORS OF THE OPTIC NERVES AND CHIASM

Although relatively infrequent, mention must be made in this review of tumors of the optic nerves and chiasm In the past, in most instances the precise diagnosis was not established until the lesion was exposed on the operating table However, in some instances the clue has been suggested if the roentgenogram reveals enlarged optic foramina and expansion forward of the anterior wall of the sella turcica and more recently Balado and Pardal by means of injection of iodized oil into the lateral ventricles have found that there is a characteristic appearance of the ventricular system in glioma of the optic chiasm There is a disappearance of that part of the third ventricle corresponding to the infundibulum and optic recess The sella turcica is normal (Fig 4)

The structure of the chiasmal gliomas seems to vary a great deal Verhoeff believes that all tumors of the optic nerve and chiasm are gliomas, though many have been reported as neuromas, myxomas fibromas, and tumors of other types Verhoeff divides the gliomas into (1) a finely reticulated type (2) a coarsely reticulated type, and (3) a spindle cell or coarsely fibrillated type

That the structures of these gliomas may vary is shown by the fact that gliomas resembling oligodendroglioma and glioblastoma multiforme have been reported Hortega finds some of these tumors have a myxomatous or fibrous appearance He believes that the gliomas of the optic nerve are polymorphous in type

Without these specific X-ray findings, the diagnosis of glioma of the optic nerves and chiasm is speculative These tumors may involve but one or both optic nerves and the chiasms as well and appear as bulbous enlargements While at first the lesion is confined within the sheath of the nerve or nerves eventually it may expand and reach beyond these limitations

When the tumor is of small dimensions the clinical expression may be represented only by optic atrophy field defects and loss of visual acuity One should remember the possibility of hysteria when there are signs only of visual defects and visual loss Such was the case in a patient a young woman, who had marked concentric contraction of the visual fields and an apparent loss in vision She had been told elsewhere that she had a tumor of the optic chiasm with no hope of relief The hysterical origin of the lesion was suspected and under a single galvanic shock the fields immediately expanded to normal and vision was restored to normal As time goes on and the tumor grows headache may develop, there may be signs of hypophyseal dysfunction with the characteristic alterations in the sella and optic foramina

As in the case about to be recorded these tumors appear most frequently in children The inevitable blindness that would follow a radical removal has placed these lesions in the inoperable class

CASE 3 A boy 12 years old, had complained of defective vision and headache He was short of stature but with no outstanding signs of hypophyseal dysfunction Except for a bitemporal hemianopsia and a bilateral optic atrophy the findings were essentially negative Operation revealed a tumor of the right optic nerve (Fig 5)

Clinical history W G aged 12 years (File No 88816 G H.) was referred to Dr P C Grant on November 10 1930, with the chief complaint of dimness of vision September 1930 the child was referred to Wills Eye Hospital because of a visual defect. He had difficulty in reading and held the print to the left side of the face He had complained of headache for 3 months, was listless and tired easily

Examination With the exception of the visual disturbances, nothing was observed in the neurological examination except hyperactive abdominal reflexes, a hyperactive left patellar reflex, and a bilateral Babinski The X ray of the head and pituitary fossa and the serological tests were negative

Ophthalmic report There was no disturbance of ocular motility Pupillary reflexes were normal, the left pupil slightly smaller The consensual reflex was present and convergence was good With ophthalmic light the field of vision in the right eye was lost except in the inferior nasal quadrant In the left eye the vision was maintained in both the inferior and superior quadrants There was a bilateral optic atrophy

Operation November 22 1931 Right transfrontal craniotomy Upon elevation of the right frontal lobe a small tumor was exposed, about 1 centimeter in diameter taking its origin from and involving the right optic nerve It seemed to rest upon the anterior clinoid process Upon further exploration the tumor seemed to involve the left optic nerve as well Two nubbins of tumor were removed from the right optic nerve and after this procedure the wound was closed

Pathological diagnosis Glioma

GROUP III TUMORS OF THE LESSER WING OF THE SPHENOID

The most common location for parasellar tumors is the sphenoidal ridge a term given to that portion of the sphenoid bone formed by the lesser and greater wings Tumors involving the sphenoidal ridge may be located either on the lesser or greater wings, but since only those located on the lesser wing may be looked upon as true parasellar tumors only those will be considered.

Histologically the most common tumor in this area, far outnumbering all others, is the meningeal fibroblastoma. At times gliomas involving the mesial aspect of the temporal lobe may spread over the adjacent sphenoid wings of the sphenoid bone but these are not primary tumors of this region Rarely an hypophyseal adenoma may expand laterally and involve the lesser sphenoidal wing, but by and large the great majority if not all of the primary tumors arising along the lesser sphenoidal ridge are meningeal fibroblastomas. These tumors are encapsulated but may be so firmly attached to the dura overlying the ridge that they cannot readily be removed *in toto* They vary in size (Figs. 6 and 7) from tumors only 1 5 to 2 centimeters in diameter and confined entirely to the ridge to others which are 4 to 5 centimeters in diameter extend forward into the anterior fossa or even backward into the adjacent middle fossa. Tumors confined to the lesser wing of the sphenoid bone are rare and give rise to few symptoms when present however the latter are quite characteristic, and if the tumor be promptly recognized it may readily be removed However when the tumor has expanded into the anterior and middle fossa, the surgical problem becomes more difficult (Fig 8) In the anterior fossa these tumors usually grow along the olfactory groove, hollowing out a place under the frontal lobe In the middle fossa they make their beds under the temporal lobe Sometimes the tumors are indented by a deep fissure where they have straddled the ridge

Their histological structure is quite uniform They present for the most part typical features of the meningeal fibroblastoma, with a well defined capsule streams and whorls of cells, with varying amounts of collagen and fibroglia. Not all are of this type however for I have in my series two specimens that are classified as hemangio-endotheliomas

Why is it that the suprasellar fibroblastomas, those arising from the tuberculum sellae and the parasellar fibroblastomas springing from the lesser sphenoid ridge occur more frequently than the fibroblastomas arising at any

Fig 6 Small sphenoidal ridge tumor

Fig 7 Medium sized sphenoidal ridge tumor with the left optic nerve overstretched.

other point on the base of the skull? As demonstrated by Schmidt and others, these tumors arise from the arachnoidal villi the histological structure of which they resemble closely Since the number of these villi is greater in the region of the sella turcica than at other points on the base of the skull, it is not surprising that these tumors occur in greater numbers in what appear to be these sites of predilection (Fig 9)

Sphenoidal ridge tumors of the lesser wing are lateral to the sella turcica, on one side or the other, and by virtue of their location may produce changes in the bony structure detectable by X-ray There may be an unilateral erosion of the sella turcica, an erosion of the dorsum sellæ, and posterior clinoid processes with destruction of the sellar floor on one side or destruction of the wing itself In some cases there may be an enlargement of the optic foramen on the side of the tumor More often there is destruction of the adjacent posterior clinoids and erosion of the dorsum sellæ Before discussing the clinical manifestations, we submit by way of illustration the following case

CASE 4 A small tumor of the left sphenoid ridge arising from the lesser wing Progressive symptoms for 1 year Bilateral primary optic atrophy Visual acuity, 20/200 in both eyes Right homonymous hemianopsia Slight right facial weakness Impairment of taste Weakness of the right hand Basal metabolic rate, minus 12 Normal intracranial pressure Sella turcica "top normal" in size, 12 by 6 millimeters

Clinical history J F, a man, aged 37 years (File No 20020), 1 year before entrance had noticed impairment of vision Vision continued to fail, but he

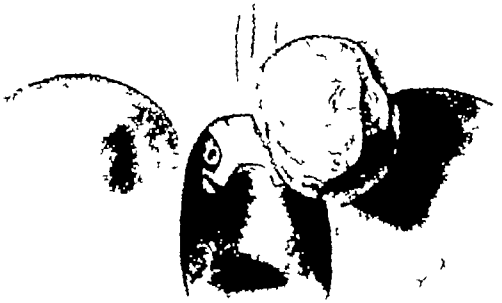

Fig 8 Large sphenoidal ridge tumor encroaching on optic chiasm, spreading into anterior and middle fossæ

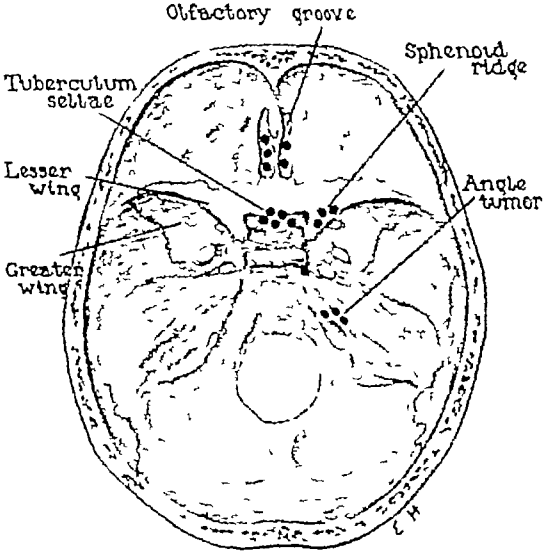

Fig 9 Base of the skull showing the favorite sites of the basilar fibroblastomas

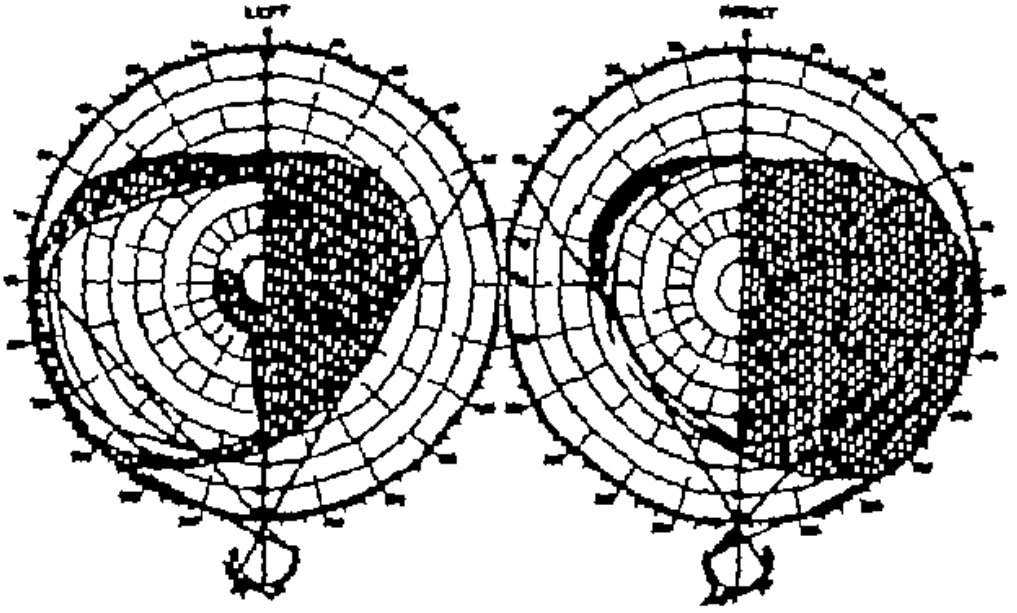

Fig Case 4 Fields before operation (October 7 1930) Vision—left eye, 20/200 right eye, 20/200 Homonymous hemianopsia extending through the fixation point

was able to work until 2 weeks before entrance to the hospital Coincident with the visual disturbances he had fleeting pains in the head These headaches were generalized, occurred about every 3 days, and showed no tendency to increase in frequency or severity During the onset of the symptoms he had noticed decreased sexual desire This had progressed to complete loss at the time of admission

Examination There was bilateral primary optic atrophy with markedly decreased visual acuity, measuring 20 200 in both eyes Studies of the visual fields revealed a clearcut left homonymous hemianopsia (Fig 10) Examination of the cranial nerves gave negative results otherwise There were slight central facial weakness on the right, slight weakness of the right arm and hand, the grip being 45 as compared with 60 on the left and slight increase in the right biceps reflex Endocrine disturbances, though not conspicuous, were present They consisted of complete loss of libido polyuria a rather pronounced gain in weight in the 3 year previous to admission, slight loss of hair smooth and silky skin, and somnolence (Fig 11)

Perhaps the most constant symptoms are the loss of visual acuity field distortions and the X-ray findings already mentioned An homonymous hemianopsia was an invariable feature in my series From this one would anticipate the location of the tumor on one or the other side of the sella turcica Vinson may

Fig Case 4 Meningeal fibroblastoma of lesser wing of sphenoid bone

Fig Case 4 Complete oculomotor paralysis in a patient with tumor of the lesser sphenoid wing

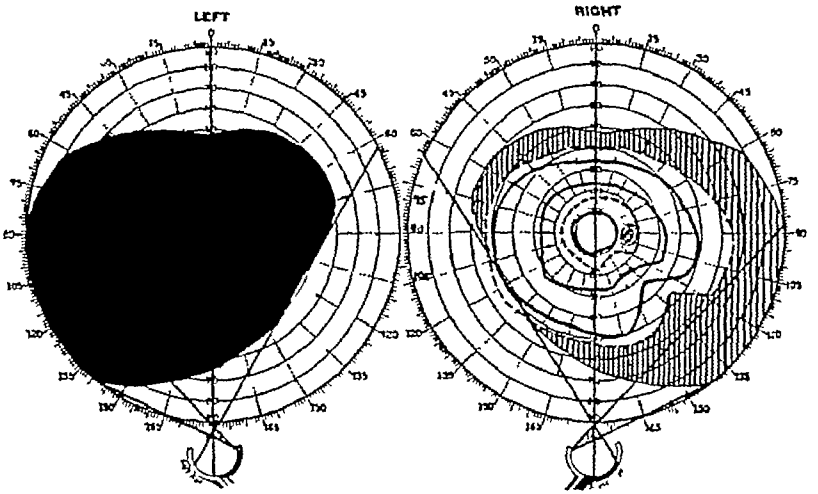

Fig 13 Case 5 Fields before operation Vision, left shadows, right 6/5—4 with correction

be seriously impaired and in all cases but one in my series there was a primary optic atrophy and in one instance a papilledema on the contralateral side and a primary optic atrophy homolateral to the lesion

In 1 instance there was a complete oculomotor paralysis (Fig 12) Among associated symptoms were noted impairment of taste hypopituitary stigmas impairment of memory, and homolateral paralysis which may be due to compression of the anterior and middle cerebral vessels

The following case differs from the former in many particulars and is cited by way of contrast

CASE 5 Middle aged man complained of pain on left side of nose for 3 years Meanwhile he developed a left exophthalmos left sided blindness and corneal hypesthesia The X ray films revealed a destructive lesion of the lesser wing of the sphenoid which at the operation proved to be, as suspected, a fibroblastoma The tumor was readily removed

Clinical history H L, aged 42 years (File No 30181) was referred by Dr T H Farrell of Utica New York to the Neurosurgical Service of the University Hospital November 13 1934 The patient was well until August, 1931, when he developed pain first in his left arm and then on the left side of the nose It was a steady constant ache From April to October, 1932, he was pain free Then his vision became cloudy, he lost 20 pounds in weight, and felt slack July 1933, he noted spells in which he could not see or hear By September 1933 his vision in the left eye was much worse and the left eye became more prominent December 1933 an exploratory operation was performed in another hospital and the operator reported thickened walls of the left orbit No tumor was found

The pain and failing vision continued and in April, 1934, he applied at another clinic for relief Here his symptoms were thought to be of functional origin

When he reported to my service the pain was still present and referred chiefly to the side of the nose His left eye was amaurotic, he had lost some 40 pounds in weight and was quite demoralized

Examination The neurological findings were few and had to do only with the left eye There was a marked exophthalmos, by measurement right 16 5, left 18 5, there was limitation of ocular movements (left), right eye vision, blind, left eye vision 6/5 Fields slight bitemporal cut (Fig 13) There was impairment of corneal sensation (left)

Roentgenogram Dr Pancoast reported that either a portion of the lesser wing of the sphenoid bone had

Fig 14 Case 5 Roentgenogram reveals destruction of the lesser wing of the sphenoid

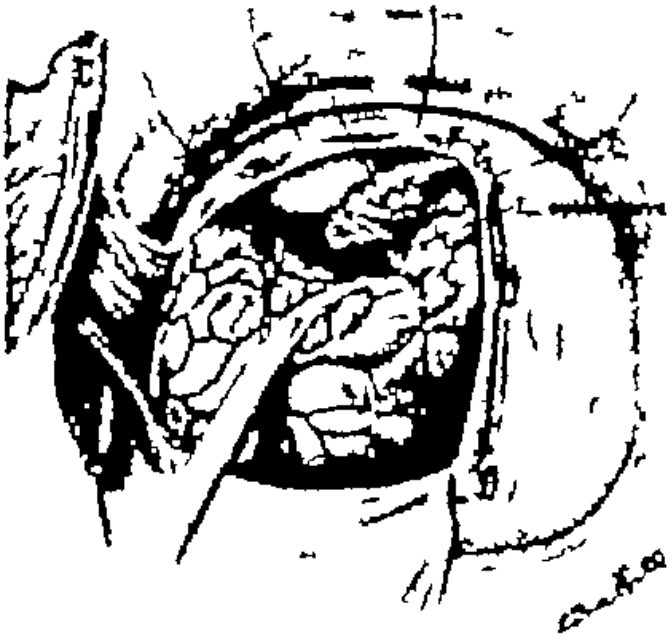

Fig 15 Case 5 Tumor of lesser wing of sphenoid surrounding left optic nerve

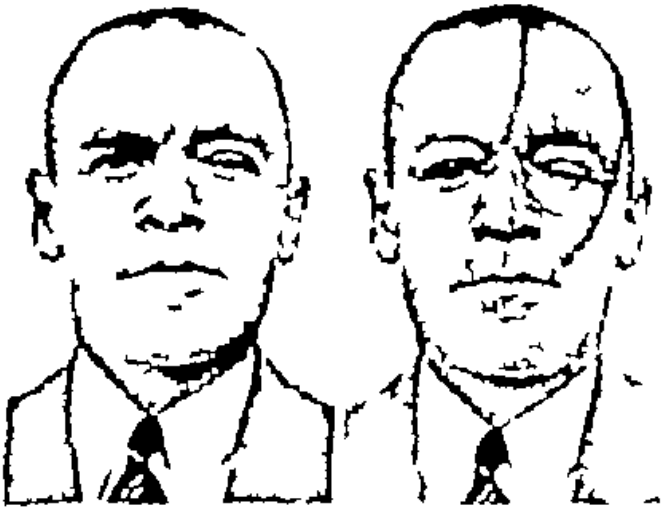

Fig 16 Case 5 Photographs of patient 3 weeks after operation Coronal incision imperceptible Hypesthetic area outlined

been removed, or that he would have to report there had been some destruction of this portion of the sphenoid wing (Fig 14)

In all other respects the examination was negative

With the prolonged history of pain referred to the left maxillary division of the fifth nerve, with the left exophthalmos, the left partial ophthalmoplegia, left blindness, and finally the X-ray evidence of destruction of the sphenoid wing, the diagnosis seemed obvious—fibroblastoma of the lesser wing

Operation November 20, 1934 The question of approach was complicated somewhat by the presence of the incision from the previous operation This difficulty was met by using our coronal incision from the tip of one ear to that of the other This flap included the earlier incision and proved a happy solution of what seemed a difficult surgical problem The incision of the first operation would have been wholly inappropriate for our exploration The tumor was exposed without any difficulty (Fig 15) Beginning in the anterior fossa above the lesser wing and passing obliquely downward, completely surrounding the left optic nerve on its way it extended into the middle fossa and stopped just over the gasserian ganglion

The tumor was oblong in shape and rather nodulated on the surface A greater portion, including the left optic nerve between the optic foramen and chiasm was scalloped out with the electrical loop and the capsule removed later by blunt dissection The tumor was quite bloodless and easily excised The dural incision was closed snugly bone flap replaced, and scalp incision closed with tier sutures

Postoperative course The postoperative course was uneventful save for an aphasia which did not appear for 48 hours and lasted only 5 days He was discharged 23 days after the operation There was an hypesthetic area corresponding to the distribution of the first and second divisions of the trigeminal nerve (Fig 16)

Pathological report Fibroblastoma

TABLE 1 SUMMARY OF FINDINGS IN FIVE CASES OF TUMORS OF THE LESSER SPHENOIDAL WING

Visual acuity	Optic atrophy	Papilledema	Fields	Roentgen findings	
				Measurements of sella turcica	Dorsum
Right eye Left eye			Left [illegible]	by mm	Eroded
Both eyes [illegible] mm	Bilateral primary		Left [illegible]	by 4 mm	Slight atrophy
Right eye blind	Right eye primary	Left eye	Left [illegible]		Complete erosion
Right eye [illegible] Left eye [illegible]	Bilateral primary		Right [illegible]	12 by mm	Negative
Left eye blind	Unilateral primary		Left eye blindness	Destruction lesser wing	

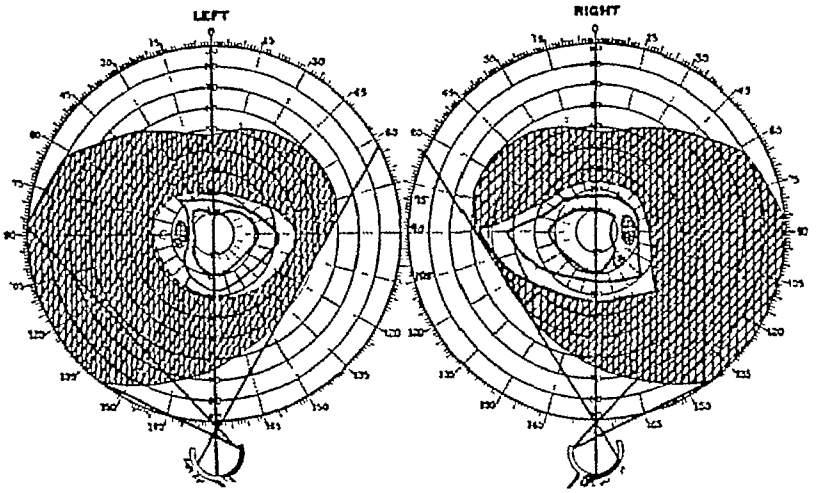

Fig 17 Case 6 Fields before operation Vision—left eye 6/9, right eye 6/9

The symptoms in this case were distinctly unilateral and in that particular the case fits into our conception of these lesser wing tumors, but there were some unusual features that deserve mention In the first place, all the symptoms were essentially focal, in the second place, there was an exophthalmos and partial ophthalmoplegia not usually observed Again, the X-ray findings admitted of but one interpretation, instead of atrophy of the clinoid processes or erosion of the dorsum sellæ there was a definite loss of substance of the sphenoid wing Finally, from the beginning and for 3 years the conspicuous symptom had been pain, pain referred to the trigeminal distribution especially that of its second division Strangely enough the true nature of the lesion had not been recognized until the patient reported to this clinic By this time optic atrophy was so well advanced that the vision of his left eye could not be restored

Generally speaking these lesser wing tumors may be distinguished from suprasellar lesions by the conspicuously unilateral picture It is not pertinent in this discussion to consider their differentiation from tumors arising from the greater wing of the sphenoid bone (See "Parasellar Tumors," Alpers and Groff)

GROUP IV SUPRASELLAR PSEUDOTUMORS

Under the caption "Cerebral Pseudotumors," I reviewed in 1930 a series of 22 cases in which the symptoms mimicked those of a solid lesion but were found to be due to a circumscribed collection of fluid beneath the arachnoid Of these 22 cases 4 suggested an hypophyseal, and 1 a suprasellar lesion The term "pseudotumor" was first employed by Nonne and since then has been variously referred to as "meningitis serosa" ' meningitis serosa circumscripta " "meningo-encephalitis serosa," ' arachnitis " and "generalized cisternal arachnoiditis " Since the pathological lesion may vary and since in a number of cases, in fact in most recorded as pseudotumor no histological studies of the arachnoid

Fig 18 Pseudotumor in the suprasellar area showing a thickened arachnoid membrane over the optic nerves and chiasm, giving rise to symptoms of a chiasmal syndrome

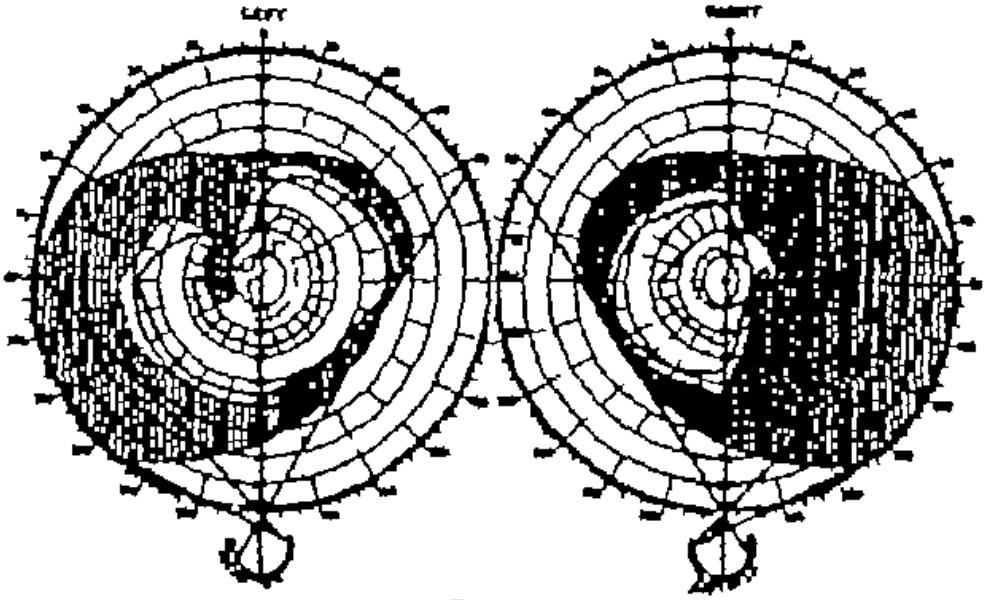

Fig. 9

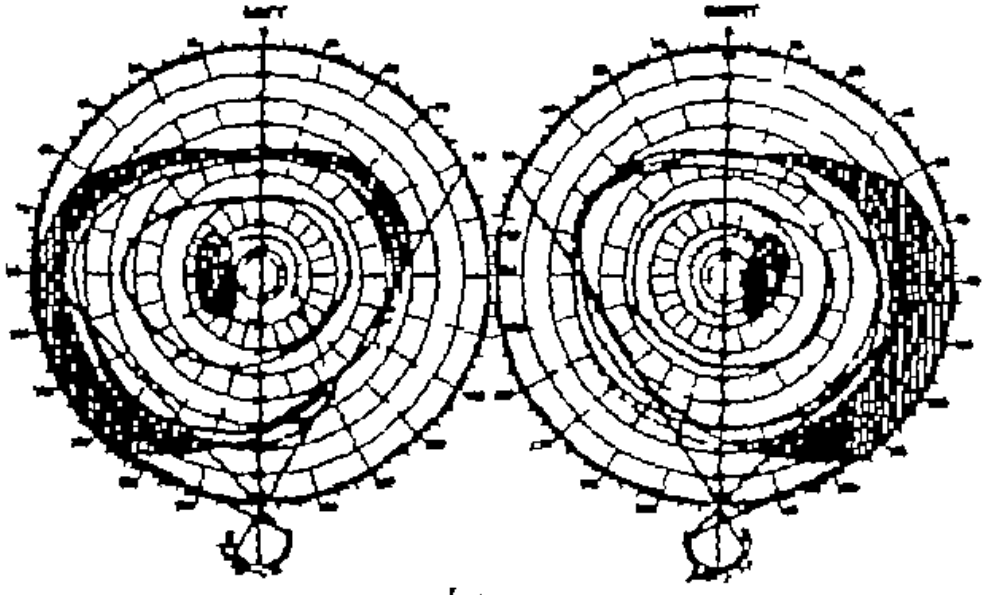

Fig.

Fig. 11

Fig. 9. Case 7. Fields before operation. Vision—left eye, 6/12; right eye, 6/12.

Fig. 10. Case 7. Fields after operation. Vision—left eye, 6/15; right eye, 6/15.

Fig. Case 7. Photograph of patient on discharge from hospital.

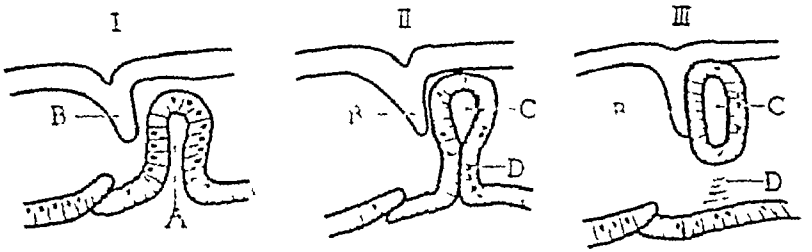

Fig. 22. Diagrammatic sketch of the development of the hypophysis from the buccal cavity. I. The original invagination from the buccal cavity. II. Communication with the buccal cavity obliterated at *D*, the structure from which the anterior lobe arises *C*. III. The remnant of stalk *D*, the anterior lobe *C* in close relation with the infundibular process *B*.

were made it seems that Nonne's term "pseudotumor" is more descriptive and should be retained.

Case 6. I. S., aged 40 years, female (File No. 13735) was first admitted to the Neurosurgical Service of the University Hospital June 19, 1928, and readmitted November, 1928, December, 1928, and April, 1930.

Clinical history. In 1920, 8 years ago, she first noticed that her vision was failing. She could read fine print at this time but was unable to see objects either to the right or left. Evidently at that time she had a bitemporal hemianopsia. Her ethmoid sinuses were drained but without any effect upon her fields or her visual acuity. In 1928, she was told her fields were becoming more restricted (Fig. 17). Her vision November, 1928, was 6/9 in each eye. There was no papilledema.

April, 1930, on readmission to the University Hospital there was some loss of her olfactory sense, vision reduced to tubular type, was right eye 6/15 and left eye 6/22. In all other respects her examination was negative.

Operation. May 12, 1930, transfrontal craniotomy, right. Under local anesthesia. Quoting from the operation notes: "There was no evidence whatsoever of a tumor either above or below the chiasm. The naked eye appearance was very much that which we have already described in other cases of pseudotumor. The arachnoid seemed quite adherent over the chiasm and at places thickened. One might well understand how the cerebrospinal fluid could be more or less pent up over the chiasm and give rise to pressure symptoms." The operative diagnosis was suprasellar arachnitis.

It is interesting to note that before the patient's discharge from the Hospital the fields had expanded and were three times as large as

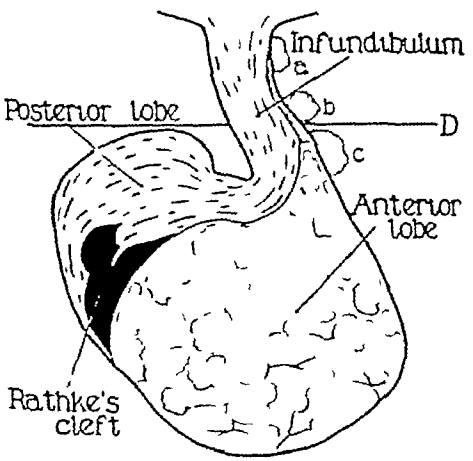

Fig. 23. Anatomical drawing to show the various constituents of the fully developed hypophysis. Note between the anterior lobe and the posterior lobe the location of Rathke's cleft.

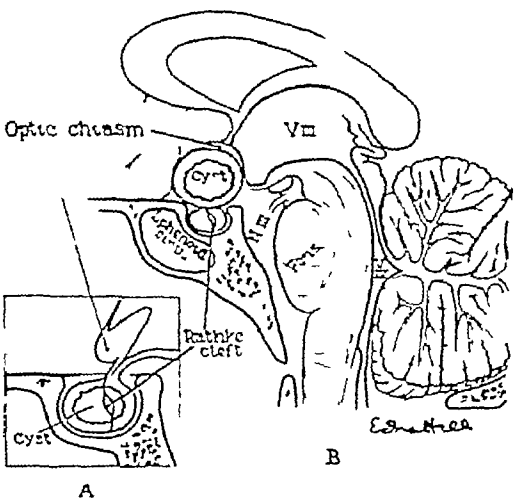

Fig. 24. A. Intrasellar Rathke cleft cyst compressing anterior and posterior lobes but causing no enlargement of sella. Note the origin from the Rathke cleft. *B*. Suprasellar Rathke cleft cyst similar in origin to inset 1 with compression of optic chiasm and only minor sellar changes.

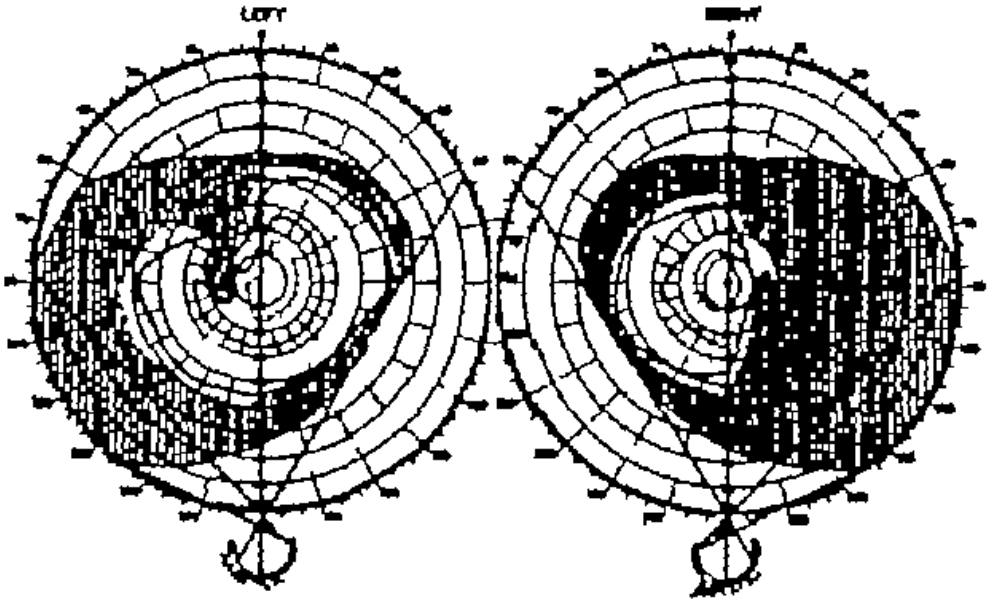

Fig. 9

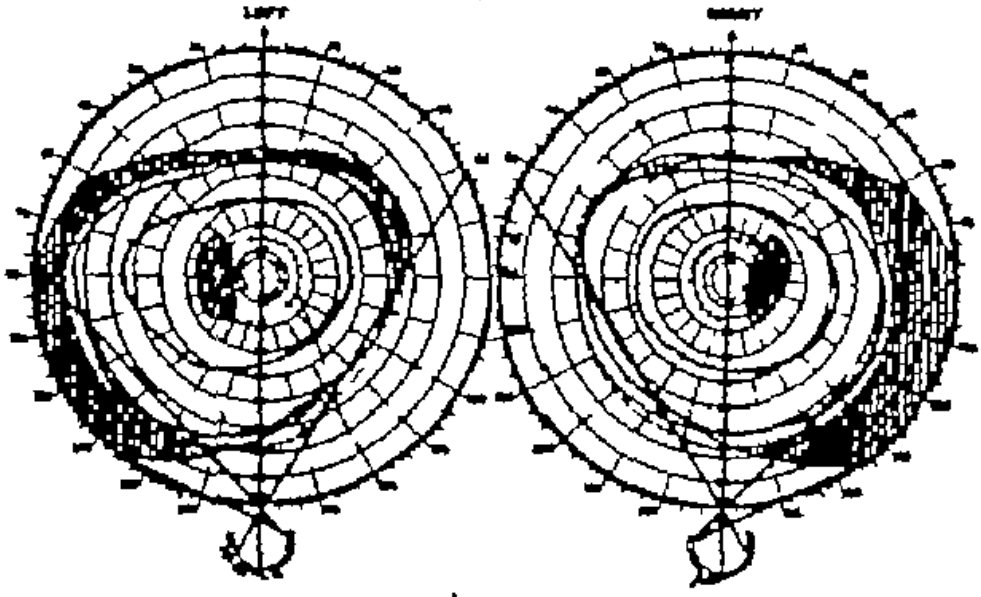

Fig. 10

Fig. 8

Fig. 9. Case 7. Fields before operation. Vision—left eye, 6/22; right eye, 6/21.

Fig. 10. Case 7. Fields after operation. Vision—left eye, 6/15; right eye, 6/15.

Fig. 8. Case 7. Photograph of patient on discharge from hospital.

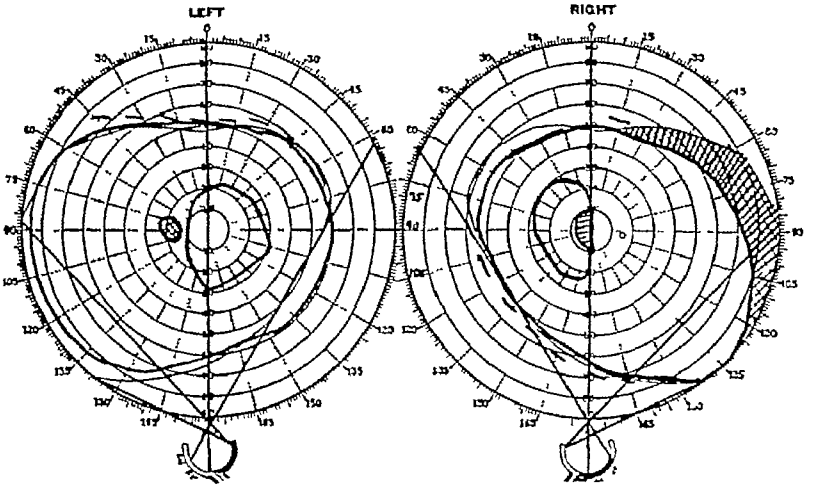

Fig 27 Case 8 Fields after operation Vision—left eye, 6/12 with correction, right eye 6/60 with correction

CASE 7 A woman in her 38th year had symptoms for only 6 months, bitemporal hemianopsia, impairment of vision, headache, vomiting and vertigo, and an enlarged sella turcica film completed the picture Operative findings, pseudotumor Immediate relief

Clinical history L M, aged 38 years (File No 30009), was admitted to the Neurosurgical Service, referred by Dr Edward Lentz, October 15, 1934, with the following history

From March, 1934, 6 months, she has had shooting pains in the occipital region and a sense of fullness in the head At times she became dizzy and had to sit down July, 1934, the headache, once intermittent, became constant. Attacks of nausea and vomiting followed She complained that though she could see the printed word she could not grasp the meaning

Examination There were no objective findings save the field distortion and the X-ray picture

There was a complete loss in the temporal field of vision in right eye and of the upper temporal quadrant in left eye Vision in both eyes was 6/22 Discs appeared normal (Fig 19)

Roentgenogram Definite enlargement of the sella turcica (14 by 11 millimeters) with encroachment upon the sphenoid sinus but without atrophy of the posterior clinoid processes The findings suggest a pituitary tumor

All other special examinations were negative

Operation November 5, 1934 Transfrontal craniotomy, right, under local anesthesia In approaching the pituitary fossa along the sphenoidal ridge it was evident there was no pituitary tumor A bluish membrane overlay the chiasm and optic nerves and confined beneath it and around the optic nerves was a large collection of fluid The membrane, presumably thickened arachnoid, was removed and the wound closed.

Operative diagnosis Pseudotumor

Postoperative course The patient's convalescence was uneventful Save for 2 days of drowsiness that often follows the pituitary exploration, the convalescence was uncomplicated Particularly striking was the widening of the fields within 2 hours of the operation and upon the patient's discharge, November 17, 12 days after the operation, the fields were nearly normal (Fig 20) and her vision was both eyes 6/15 The headaches had disappeared (Fig 21)

When there are signs of hypophyseal dysfunction one may consider with perfect propriety a suprasellar adenoma Such was the case in a patient (File No 2759 N S) who had obesity, evidence of femininity, a basal metabolism of minus 22, and an homonymous

Fig 28 Case 8 Photograph of patient 3½ years after operation

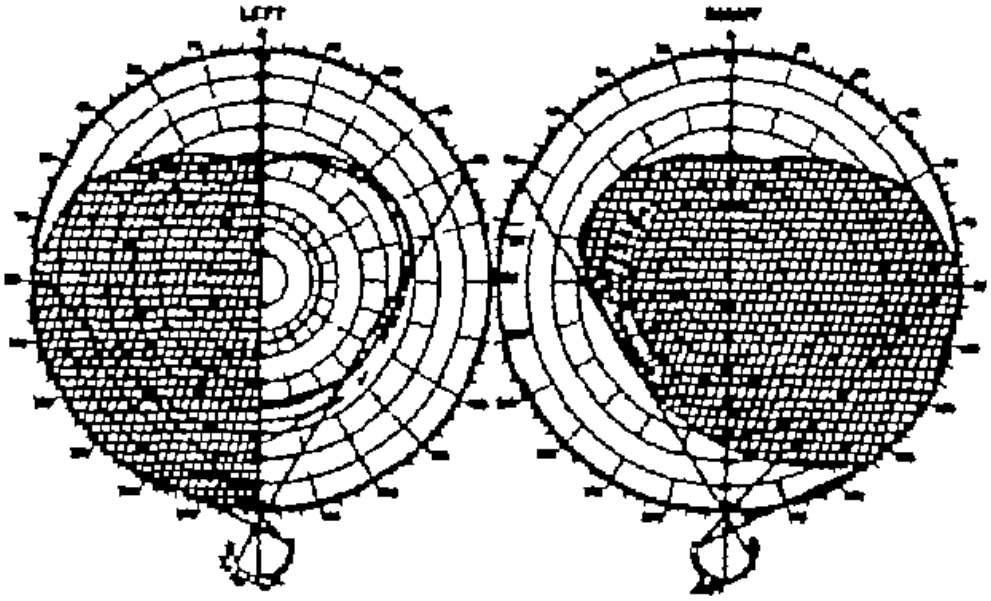

Fig 15 Case 8 Fields before operation Vision—left eye, 3/60 right eye, shadows

before the operation. May 1934 when last heard from the fields were reported as wider than on the previous examination

My experience with the surgical treatment of pseudotumor or arachnoiditis has been most satisfactory at least to the extent that with one exception I have in no instance been called to operate a second time

The etiology of this condition is obscure One may postulate a focus of infection as in the case above cited when the patient had had an ethmoiditis but in most instances infection does not seem to have been a factor The diagnosis must finally be verified by the operation

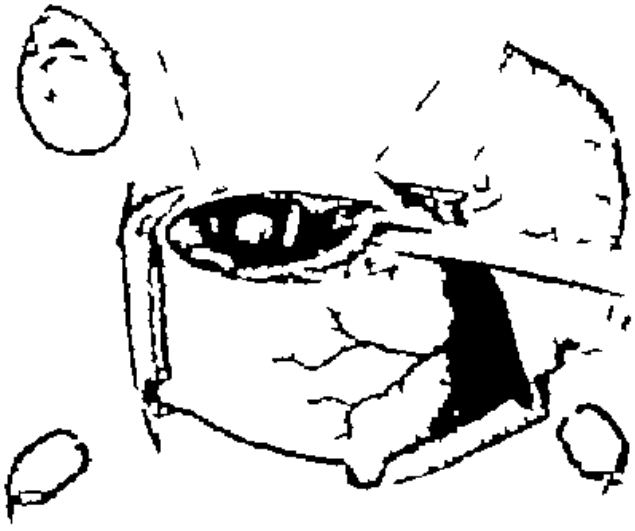

Fig 16 Case 8 Drawing at operation Tumor of Rathke's cleft

findings thickening of the arachnoid with adhesions, and a circumscribed collection of fluid in the cisterna chiasmatis (Fig. 18)

In addition to the increased amount of fluid in the cisterna chiasmatis I have found the optic nerves surrounded and constricted by the thickened pia arachnoid and have made incisions in the membrane to relieve the constriction

From the standpoint of diagnosis one must depend largely upon the visual phenomena, the loss of visual acuity and the field distortions, and hemianopsia or as in the preceding case a concentric contraction of vision This patient however may in the first instance have had a bitemporal hemianopsia as at first she was unable to see objects in either temporal field The provisional pre-operative diagnosis may be quite reasonably a suprasellar fibroblastoma I know of no means of differentiating a suprasellar fibroblastoma from a suprasellar arachnoiditis unless it be by means of an encephalogram In the latter case the cisterna chiasmatis may be enlarged should the spaces not be entirely shut off by adhesions and in the former the cistern would not be portrayed

The following case is of no little interest because the symptoms were only of 6 months duration and the sella turcica was definitely enlarged The picture would have been readily explained by a pituitary adenoma

hemianopsia The case proved to be one of pseudotumor No tumor was found at operation and the end-results have been most gratifying At least, April 4, 1930, 6 years after the operation his vision was right eye 6/15, left eye 6/9, as compared with right 1/60 and left 4/60 before the operation He said he felt better than he had for 21 years He weighed at the time of operation 210 pounds and at the time of this report, 213 pounds

Briefly, then, suprasellar arachnoiditis may be said to be characterized by failing vision, optic atrophy, an hemianopsia or concentric contraction of fields, usually with no enlargement of the sella turcica, but in some instances with signs of hypophyseal dysfunction

GROUP V TUMORS OF RATHKE'S CLEFT

There is good reason for the recognition of a separate group of tumors to be known as the tumors or cysts of Rathke's cleft In the past the term "Rathke pouch tumor" has been used loosely to designate almost any congenital suprasellar tumor, and chiefly for the hypophyseal stalk tumors The term so used is obviously a misnomer, for the stalk tumors are not truly tumors of Rathke's pouch or of its adult counterpart, the Rathke cleft in the adult human hypophysis

The term "Rathke's pouch tumor" for obvious reasons, as we shall see later, should give way to "Rathke's cleft tumors " In this brief communication we shall endeavor so to define the Rathke's cleft tumor anatomically and pathologically that it may be identified and acknowledged as a definite pathological entity and may be differentiated from any other hypophyseal or parahypophyseal lesion

Rathke's pouch in the terms of the anatomist is an invagination from the roof of the primitive oral cavity In the process of development it becomes constricted off and a sac is formed with a narrow stalk (Fig 22) The sac eventually closes and the stalk, originally connected with the mouth, usually disappears This stalk in some cases persists, as does the thyroglossal duct—the analogy is quite close—and from the epithelial rests the stalk tumors have their origin

The original Rathke's pouch becomes converted into a solid structure, the pars anterior or the glandular lobe of the hypophysis But there remains between the pars anterior and the pars posterior or processus infundibuli *a small cleft* (Figs 23 and 24) *This is all that remains of the original pouch, as described by Rathke, and it is from this cleft that the tumors we discuss originate In this sense it would seem proper to designate them as Rathke's cleft tumors*

For purposes of illustration, we present the following case

CASE 8 The patient, a male of 52 years, had had frontal headaches and eye trouble for 2 years Blindness of the right eye for 4 months Temporal hemianopsia in left eye Blurring of discs Erosion of right sphenoidal ridge Transfrontal craniotomy with disclosure of cyst presenting between optic nerves Histologically a true Rathke's cleft cyst with columnar ciliated epithelial lining

Clinical history C B (File No 22337) was referred to the Neurosurgical Service of the University Hospital July 27, 1931, by Dr R D Wallace About 2 years before his admission he began to have frontal headaches He was treated for sinus disease and in 11 weeks his headaches disappeared They returned 8 months before his admission to the hospital and persisted from this time on They were dull, constant and mostly frontal, though for 2 months before entrance into the hospital he had pain in the left temple

In 1929, about 2 years before admission, he began having trouble with his eyes Objects were at first blurred and indistinct His vision became steadily worse until he lost it completely in his right eye 4 months ago

Examination revealed total blindness of the right eye, temporal hemianopsia in the left (Fig 25) and yellow optic discs which were blurred along their margins There were no other positive findings The spinal fluid pressure was 150 millimeters of water The blood and spinal fluid serology were entirely negative

Roentgen observations The roentgenogram of the

Fig 29 Left, A portion of the cyst wall showing the ciliated columnar epithelium, *A*, with transition to unciliated cuboidal, *B*, and flat cells, *C* Hematoxylin and eosin stain. Right, A high power view showing the stout cilia projecting from the columnar cells Hematoxylin and eosin stain

Fig 30 Left, Transition epithelium of a pseudosquamous type in the cyst wall. Hematoxylin and eosin stain. Right, The same area under higher power showing the tendency to stratification and squamous-like cells in the lower layers Hematoxylin and eosin stain.

Fig 31 Case of Fulstow Left, A large Rathke cleft cyst of the intrasellar type compressing the anterior and posterior lobes, particularly the latter Right, Part of the cyst is lined with a ciliated columnar epithelium

Fig. 30

Fig. 1

Fig. 31

GROUP VI HYPOPHYSEAL STALK TUMORS

In the classification we have adopted of lesions that are indirectly related to the hypophysis, what we have chosen to designate "hypophyseal stalk" tumors constitute a not inconsiderable number and these may be differentiated from the preceding group, the "hypophyseal cleft" tumors, by certain pathological and clinical characteristics For illustration we have selected 4 cases from our series

In the first case, a boy of 16 years (File No 19387) with the stature of a 10 year old child, the outstanding features were arrest in growth, convulsions, somnolence, headache, defective vision, primary optic atrophy, a bitemporal hemianopsia, the roentgenogram revealed atrophy of the dorsum sella and convolutional atrophy, the floor of the sella was markedly depressed and there was the shadow of a calcified tumor suprasellar

In the second case, the patient, a child, though in her eighth year, was said to have had headache since she first was able to talk There were no neurologic signs save an abortive bilateral ankle clonus Of hypophyseal stigmas a tendency to adiposity, including a protruding abdomen, prominent breasts, and tapering fingers were readily recognized The basal metabolism was minus 6 The right eye was amaurotic and the temporal field of the left eye was obscured, the discs had the appearance of a subsiding choking with atrophy, they were gray with obscured margins In the roentgenogram the clinoid processes had disappeared, the floor of the sella was eroded, the sella turcica was somewhat enlarged, and above and behind was a calcified shadow 4 by 6 centimeters in diameter

In the third case, the predominant symptoms were those of increased intracranial pressure, headaches, projectile vomiting, and papilledema There were no sensory, motor, or reflex phenomena There was convolutional atrophy but no apparent involvement of the sella turcica Vision in the right eye was 6/21, in the left 6/12 and the discs showed a papilledema of plus 5 diopters The fields were normal The child, aged 12 years (File No 9169), was short for her years, there was evidence of adiposity, the basal metabolism was minus 4 A year after a subtemporal decompression the child suddenly died and a large calcified tumor was found extending from the anterior prefrontal space to the anterior margin of the pons

The first three cases cited were those of children, 8, 12, and 16 years, respectively, and the fourth is included because of the contrast in ages This patient, a woman in her thirty-third year (File No 10028) had complained of headache for over a year Her symptoms might readily have been cited as those of an hypophyseal adenoma amenorrhea, adiposity, basal metabolism minus 15, a bitemporal hemianopsia with deteriorating vision (2/60), but the sella turcica was not enlarged A cystic tumor beneath and behind the optic chiasm was found and removed and the patient is alive and well 8 years later

Altogether there are in our files 16 cases of these so called hypophyseal stalk tumors The *life history* of these tumors has a wide range In about half it was a matter of months, from 4 to 10, and in the others a matter of years, from 1 to 7 For example, in 1 of the cases cited (Case 2), a child of 8 years, the patient had complained of headache since she was old enough to talk In another (Case 1) the child had had headache and somnolence for 3 years, and his growth from the beginning had been arrested The first symptom in 6 cases was headache, in 2 headache and dimness of vision, in 1 headache and somnolence, in 1 dimness of vision, in 3 arrest of growth, and in 1 convulsions

The *basal metabolism*, when recorded, was always subnormal In fact, in the vast majority of lesions, when hypophyseal function is disturbed, the metabolic rate is below rather than above normal This applies even to primary hypophyseal adenomas Hence, the metabolic rate is of little or no significance in the differentiation between parahypophyseal and primary hypophyseal lesions

As to the *sex* and *age* it so happens that two-thirds of our patients were males This is a matter of little significance But, as to age, one would expect when dealing with lesions arising from congenital anlage, that the majority of patients with stalk tumors should be children or adolescents This supposition is quite in conformity with the facts Of 14 cases analyzed, 9 were between the ages of 7 and 17, 2 were in the third decade, 2 in the fourth decade, and 1 in the sixth For purposes of comparison, remember that 70 per cent of the stalk tumors developed in patients under 20 years of age, whereas 84 per cent of the same number of adenomas were found in patients over 20 years of age Age, therefore, may give a clue to the differential diagnosis of the various groups of tumors in this region, if it be accepted that the majority of stalk tumors appear in children, that adenomas are unusual before the twentieth and suprasellar fibroblastomas before the thirtieth year

When considering the *visual disturbances* of stalk tumors, one must bear in mind the location of the anlage from which these tumors originate When tumors arise from the lower

skull showed some erosion of the right sphenoidal ridge. The pituitary fossa measured 11 by 8 millimeters and showed no erosion or enlargement.

Operation July 29, 1931 Right transfrontal craniotomy avertin anesthesia The usual dual flaps were reflected as for pituitary exploration It was apparent that there was an increased intracranial pressure and, as the frontal lobe was elevated, an unusual amount of cerebrospinal fluid was evacuated This so reduced the pressure that a clear view could be had of the whole anterior fossa from right to left. Presenting between the optic nerves was a bluish membrane, evidently a cyst wall (Fig 26) This was readily freed from both the right and left optic nerves and 8 cubic centimeters of a brownish fluid was evacuated from the cyst cavity With this the cyst walls collapsed, leaving a considerable space between them and the optic nerves The chiasm was displaced backward and the distance from the optic foramina to the chiasm was at least 3 centimeters (Figs 27 and 28)

The walls of the Rathke s cleft cyst usually are lined with a columnar epithelium from the full surface of which there project stout cilia, usually several from one cell (Fig 29) The cytoplasm of these cells is similar to that of the goblet cells but contains no mucin. It is quite vacuolated and mucoid-like. The nucleus usually at the bottom of the cell is round, heavily chromatinized and single There are basal bodies at the base of the cilia This columnar epithelium may be followed into transitional cuboidal and flat cells neither of which possess cilia Some times there is in the tumor wall a poorly developed squamous epithelium (Figs 30 and 31) suggesting the possibility of a transition of these cysts into the stalk tumors The rest of the tumor is composed of a vascular and fibrous bed the latter of rather stout proportions

It may be that these cysts are not always lined with a ciliated epithelium. There is an occasional *thin walled cyst lying in the supra-sellar region which is lined with a flattened* cell similar to the type of cell seen in the transition areas of the ciliated cyst Due to the pressure of fluid within the cyst, it is quite possible that the cells, originally ciliated and columnar have lost their cilia and become flattened

The evidence for the origin of these cysts from the remnants of the Rathke pouch lies in the finding of Duffy that the Rathke cleft cysts are lined by a cylindrical epithelium which is often ciliated and in the fact that ciliated cells in the Rathke cleft of the adult hypophysis are found in a small proportion of cases, about 1 in 50 or less. Ramuseen found them in only 2 of 300 hypophyses The origin of these ciliated cells is not very clear However we believe that from such cells may be traced the origin of the tumor which we designate as a Rathke cleft cyst.

Only 1 such tumor has been found in my series of hypophyseal tumors (see Case 6) but it is probable that more will be disclosed now that we have a more precise idea of their nature. Theoretically cysts of Rathke s cleft should be found within the sella because of the position of the cleft remnant between the anterior and the posterior lobes. Such a cyst has been described by Fulstow who found a large cyst in the hypophysis between the anterior and posterior lobes in a man of 48 with glandular symptoms but no ocular manifestations The hypophysis was about three times normal in size The cyst within it was lined with stratified squamous epithelium with long papillary projections on which a low ciliated columnar epithelium could be seen Some of the cells contained mucin In all its characteristics, except for the papillary projections, the cyst resembles the cyst for which we have reserved the term Rathke s cleft cyst. Such cysts may not be rare and it is possible that the simple cysts of Duffy for example, fall into this group Hortega describes microscopic cysts lined with a cylindrical epithelium which may be ciliated or non ciliated and he too believes these cysts are derived from Rathke s pouch We urge that the term Rathke pouch tumor be abandoned and for the reasons given the term Rathke s cleft cyst be substituted.

It should be quite apparent that in many instances it will be quite impossible to determine by the clinical picture before the operation what the nature of the lesion may be. One might readily mistake a Rathke s cleft tumor for a primary hypophyseal tumor should the cyst be intrasellar or for an extrasellar adenoma should the cyst not be contained within the confines of the sella turcica. At the operation the Rathke s cleft lesion will be found to be prechiasmal and cystic in character

TABLE II—THE INCIDENCE OF ENDOCRINE DISTURBANCES WITH RELATION TO AGE

Case	Age	Dwarfism	Somnolence	Adiposity	Sexual defect	Femininity	Polyuria	Amenorrhea	Emaciation	
1	7	plus					plus			Under 20 years of age
2	8			plus						
3	9		plus	plus	plus	plus				
4	12	plus	plus			plus				
5	12	plus		plus						
6	15	plus	plus		plus		plus		plus	
7	15	plus			plus					
8	16		plus		plus					
9	17	plus				plus				
10	25		plus							Over 20 years of age
11	28		plus	plus		plus				
12	33							plus		
13	38									
14	50			plus			plus			

more lower anlage direct pressure and primary optic atrophy

There are in a few instances associated or *neighborhood symptoms,* and here and there symptoms of extraneous origin not related to either the hypophysis, the discs, or the fields In this category are included visual hallucinations (3), auditory hallucinations (1), deafness (3), tinnitus (1), vertigo (1), diplopia (1), loss of associated movement (1), inequality of pupils (1), and, in several, signs of frontal lobe invasion, such as defective memory, psychosis, delusions, jocularity, irritability, viciousness, mental apathy, and depression

Because of the varying location of these tumors along the stalk with relation to the sella turcica *the roentgenograms* present various pictures Thus, the sella turcica was moderately enlarged (4), markedly enlarged (4) There was atrophy of the dorsum sellæ, moderate (6) or marked (5) Convolutional atrophy (4) was an indication of prolonged intracranial pressure The most significant X-ray evidence as concerns the differential diagnosis, is calcification Calcification was noted in half of the series and the resulting shadows may appear as irregular areas scattered throughout the tumor or as a marginal shadow following the outline of a calcified cyst wall This combination—calcified shadows, endocrine disturbances, field distortions with alterations of the discs—especially in young people bespeaks with reasonable certainty a stalk tumor

The following are 4 illustrative cases referred to in abstract at the beginning of the section on hypophyseal stalk tumors

CASE 9 *Summary* Always undeveloped, the patient was admitted in his sixteenth year Somnolence, headache, ptosis (left), and convulsions were the outstanding symptoms At operation a large cystic tumor was revealed

Clinical history C M, a boy, aged 16 years (File No 19387), was admitted to the Neurosurgical Service of the University Hospital on June 18, 1930 His father was subject to convulsions, his mother was living and well, there were no brothers or sisters He had always been underdeveloped Three years previously, he became backward in school, refused to study, complained of headache, and was sleepy most of the time One year before admission, vision began to fail In April, 1930, he had three convulsions, in each of which he lost consciousness

Neurologic status Though 16 years of age, the child's stature was that of a boy of 10 years (Fig 34) There were no neurologic signs other than ptosis of the left eyelid. There were no hypophyseal stigmas other than arrested growth, and at times somnolence

Ocular disturbance Vision in the right eye was 6/60, in the left eye, 6/30 The fields showed bitemporal hemianopsia Primary optic atrophy was present

Roentgen observations There were convolutional atrophy, with widening of the sutures, the shadow of a calcified tumor (Fig 35), and almost complete atrophy of the dorsum sellæ and the posterior clinoid processes The floor of the sella was markedly depressed

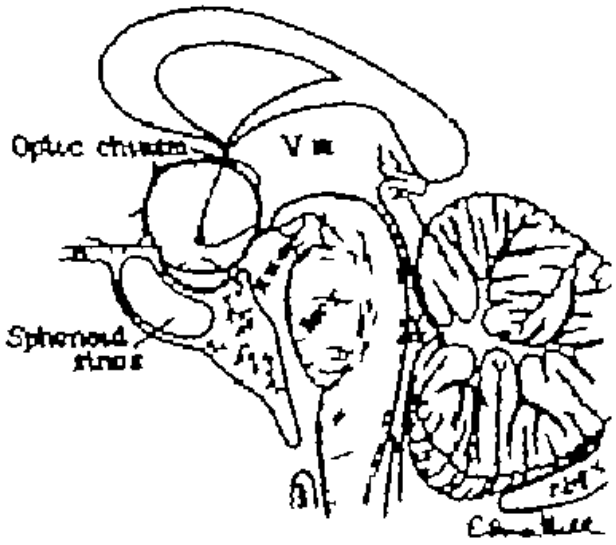

Fig 32 Hypophyseal stalk tumor arising from lower rest eroding the sella, compressing the optic chiasm and nerves

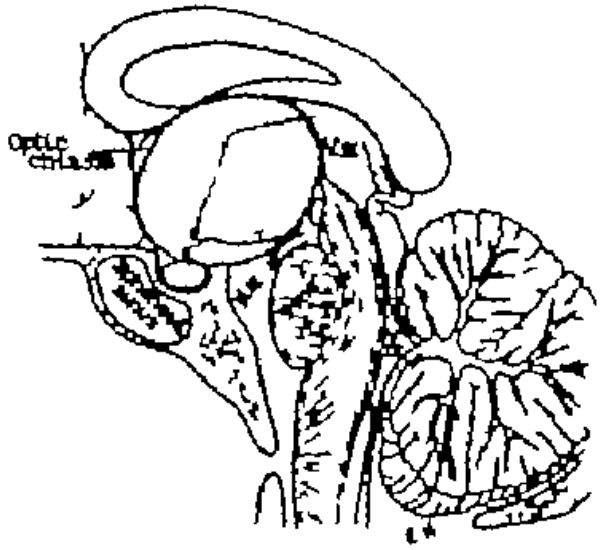

Fig 33 Hypophyseal stalk tumor chiefly retrochiasmal, arising from upper cell rest, invading third ventricle, compressing optic chiasm, slightly eroding sella.

epithelial anlage (Fig. 32) one finds a primary optic atrophy and when from the upper epithelial anlage, a papilledema with a secondary optic atrophy It is not always possible to determine at the operation from which of these two anlagen the tumor arises, but we have assumed that when the tumor was prechiasmal the tumor arose from the lower anlage and when retrochiasmal, from the upper anlage (Fig 33) This would seem to be borne out by the facts In all cases but one of primary optic atrophy the tumor presented prechiasmally and in most (5 of 7) of those described as retrochiasmal there was a secondary postpapilitic atrophy

As to the *visual fields* of 7 tumors prechiasmal the fields were described as follows 3 temporal hemianopsia of one eye, 1 concentric contraction 1 bitemporal quadrantanopsia and 2 bitemporal hemianopsia Whereas of 6 tumors manifestly retrochiasmal the fields were as follows 1 binasal hemianopsia 1 bar rel vision 1 normal fields and 2 homonymous hemianopsias.

Summarizing the various fields of the entire series of stalk tumors there were

Temporal or bitemporal hemianopsias	6
Bitemporal quadrantanopsias	
Homonymous hemianopsias	2
Binasal hemianopsias	
Concentric contraction	
Normal fields	
Amaurosis	
	4

As one might anticipate, because of the proximity of the stalk tumors to the sella turcica and the resulting pressure on the hypophysis, *endocrine disturbances* of one kind or another form part of the clinical picture (see Table II)

These endocrine disturbances are more constant in the younger than in the older patient. The most common of them was arrest of growth and the next most common somnolence. In addition to dwarfism (7) and somnolence (6) there may be adiposity (5) sexual defects (4) femininity (4) polyuria (3) amenorrhea (1) and emaciation (1) Generally speaking the endocrine features are those of the Froelich type. Gigantism or acromegaly were conspicuous by their absence.

One might anticipate signs of *intracranial pressure* when the tumor encroaches upon the third ventricle and establishes a ventricular block hence headache vomiting and papilledema Headache and vomiting were common to all whereas papilledema was observed only three times in the series

One must divine the effects of indirect pressure such as headache vomiting, and papilledema and secondary optic atrophy from that of direct pressure, primary optic atrophy Again, we must presume that tumors from the upper anlage are more prone to cause ventricular blocks with consequent increased intracranial pressure whereas tumors from the

Sublemporal decompression This operation, preceded by a ventricular estimation (by Dr F C Grant), was performed on September 24 Only 15 cubic centimeters of fluid obtained from the left ventricle and 8 cubic centimeters from the right Apparently there was no hydrocephalus

Postoperative course Convalescence was uneventful, and the patient was discharged on October 4 At that time the papilledema measured 4 diopters in the right and 3 5 diopters in the left eye Three months later the child was readmitted to the hospital and while under observation suddenly died with signs of medullary compression

Autopsy At autopsy a large tumor was found at the base of the brain with all the characteristics of a stalk tumor (Fig 39)

CASE 12 A well developed woman, aged 33 years, had complained of headaches for over a year There were a bitemporal hemianopsia and amenorrhea, but the sella turcica was not enlarged Eight years after the removal of a cystic tumor beneath and behind the chiasm, the patient was well Benefit followed the administration of thyroid extract

Clinical history K A K., a woman, aged 33 years (File No 10028), was referred to the neurosurgical service of the University Hospital by Dr Raymond H Bloss and Dr William G Spiller, on December 16, 1926 The previous medical and family history was unessential In October, 1925, the patient began to have headaches, at first dull but constant, later becoming very severe and occurring at intervals of several days They were referred to the midfrontal region, with much pain over the right eye In June, 1926, she suddenly became aware of failing vision and in August, she had the first vomiting spell On one occasion she had diplopia On December 4, vision became much worse and on December 5, for the first time she was unable to read She had been receiving courses of roentgen treatment, but the fields continued to contract and the sight to fail

Neurologic status The patient was well developed and moderately obese Her average weight for the past 10 years had been from 150 to 155 pounds (68 to 70 kilograms) There were no sensory or motor disturbances The reflexes were normal

Cerebrospinal fluid The pressure was 182 millimeters, the fluid contained 4 lymphocytes, the Wassermann reaction was negative Globulin was not increased

Roentgen observations The pituitary fossa measured 10 millimeters in the anteroposterior and 5 millimeters in the vertical plane (Fig 40)

Hypophyseal stigmas The basal metabolic rate was minus 15 The menses had been regular until 3 months before admission

Ocular manifestations Vision in each eye was 2/60 The fields showed practically a bitemporal hemianopsia, although vision was not wholly lost in the upper quadrant of each temporal field

Right transfrontal craniotomy December 20, 1926 The tumor presented prechiasmally but extended beneath and behind the chiasm It contained straw colored fluid A considerable portion of the cyst wall was removed and the wound closed.

Postoperative course The patient recovered from the operation and 8 years later has no signs of recurrence (Fig 41)

Histological report The tumor was a typical stalk tumor, often styled adamantinoma It was composed of the typical branching epithelial tree, with the basal ameloblastic layer, extensive stroma, cysts and calcium deposits in the thick fibrous capsule

THE PATHOLOGY OF HYPOPHYSEAL STALK TUMOR

Of all the tumors included in this collective review the hypophyseal stalk tumor enjoys greater distinction than any other Aneurisms, pseudotumors, fibroblastomas, and adenomas in this region can claim no distinctive features The same cannot be said of the Rathke's cleft tumor and the hypophyseal stalk tumor Hence we will discuss at greater length the pathological features of this group

These tumors arise from the remains of the Rathke pouch After the Rathke pouch has lost its connection with the buccal cavity there remains behind a so called duct composed of stratified epithelium representing the former connection with the buccal cavity This duct has been called the "craniopharyngeal duct" but, as stated in my introductory remarks erroneously so, and we have elected to designate it as the "hypophyseal stalk" and will refer to the tumors originating therefrom as "hypophyseal stalk" or simply as "stalk tumors"

The cells composing this duct may disappear completely or groups of them may be carried along with the anterior lobe of the hypophysis and be implanted along the superior surface of this lobe near the diaphragma sellæ or along the infundibulum at its union with the tuber cinereum at the base of the brain The frequency with which these epithelial rests occur is shown in the investigation of Susman, who found 71 of 230 adult human hypophyses or 30 4 per cent with epithelial rests An even higher incidence is reported by Carmichael who found them in 39 1 per cent of adult hypophyses The majority of these cell rests were epithelial in structure similar in histological structure to

Metabolism The basal metabolic rate was minus 37

August 26 1930 the patient was readmitted in a state of stupor Dr Grant removed 20 cubic centimeters of a dark brown fluid from the cyst, without any relief Dehydrating agents seemed of no avail, and the patient lingered in a state of unconsciousness for 8 weeks and died on October 6

Pathological report The tumor extended from the frontal lobes to the pons (Fig 36) It was almost completely calcified and cystic The middle cerebrum had been compressed with resultant softening of the cerebrum on both sides Histologically this was a typical stalk tumor similar in its characteristics to the other tumors except that the cyst formations were very numerous and calcification was extremely extensive involving almost all parts of the tumor

CASE 10 A girl, aged 8 years, had had daily headaches for years in the past month vision had almost failed, and for 8 days headache had been intense and vomiting incessant A large calcified tumor was found and in part removed The patient was discharged 19 days after operation

Clinical history L E H a girl, aged 8 (File No 7042 N S) was referred to the neurosurgical clinic by Dr J L McKee, on November 13 1925 The mother said that the child had had a headache every day since she could talk The attacks lasted about an hour and a half, and little attention was paid to them But for the 8 days preceding admission the headache had been intense and vomiting incessant For a month vision had been failing, until at the time of admission the child could not recognize her playmates

Neurologic status Apart from an abortive ankle clonus on both sides, there were no neurologic signs except those to be recorded

Hypophyseal stigmas There was a tendency to adiposity protruding abdomen, prominent breasts, and tapering fingers The basal metabolic rate was minus 6

Ocular disturbances The left eye showed a temporal hemianopsia vision was limited to counting fingers The right eye was blind The discs had the appearance of a subsiding choking, with atrophy they were gray with blurred margins

Roentgen observations There were destruction of the clinoid processes, erosion of the floor of the sella and some enlargement of the sella A large calcareous deposit was seen extending backward and upward it was about 4 centimeters in diameter

Craniotomy On January 15 1926 a transfrontal craniotomy was performed on the left side On reflection of the flap, the dura was exceedingly tense, but fortunately a dilated ventricle was found and with its evacuation the pressure was entirely relieved, so much so that the frontal lobe of its own weight fell away sufficiently to expose the region of the chiasm

The tumor was readily seen, presenting psychically The left optic nerve, first seen, was on the stretch and ribbon-like The center of the tumor seemed cystic, and about 1 cubic centimeter of fluid was evacuated Through a capsular incision the cavity was curetted, but little tissue was recovered The capsule was then freed from the chiasm and optic nerves, and as much as could be easily detached was removed When finished, there presented in the sella a cavity measuring approximately 2 by 2 5 centimeters in diameter

Postoperative course In the convalescent period vomiting persisted The child did not react well The general condition was not especially satisfactory and on January 25, 12 days after the operation, the child was taken home The asthenia continued, and the child died on February 1

Histological report The tumor was a typical stalk tumor with a well defined ameloblastic layer extensive stroma, and calcium deposits Spicules of calcium were found scattered through the tumor No formation of bone was seen anywhere There were rather extensive areas of degeneration everywhere throughout the tumor chiefly in the stroma No glial tissue was found

CASE 11 A girl, aged 12 years (File No 9169) was under observation for a year with signs of increased intracranial pressure and atrophy of the dorsum sellæ, headache, vomiting, choked discs and arrest of growth and adiposity Subtemporal decompression with temporary relief With recurrence of symptoms the patient died suddenly 2 days after readmission A large stalk tumor (adamantinoma) was found at autopsy

Clinical history A. G a girl, aged 12 (File 9169) was referred to the neurosurgical service of the University Hospital by Dr L F Appleman, on September 15 1926 For the ten months preceding admission the child complained of headaches, at first not severe and only once a month On the day before admission it was discovered at the Wills Eye Hospital that she had choked discs, and she was referred to this service Apart from projectile vomiting, of 6 months duration, there had been no symptoms

Neurologic status With regard to the motor and sensory mechanism, examination gave entirely normal results There were no signs suggesting a lesion either of the cerebral or of the cerebellar hemispheres

Endocrine stigmas The child was short for her age There was a tendency to adiposity with a protuberant abdomen and prominent breasts (Fig 37) The basal metabolic rate was minus 4

Roentgen observations These showed convolutional atrophy without enlargement of the pituitary fossa (Fig 38)

Ocular disturbances The fields were practically normal Vision in the right eye was 6/21 in the left eye 6/12 Papilledema in both eyes measured 5 diopters

As there was no positive evidence of an hypophyseal lesion and there were highly choked discs, the indication for a subtemporal decompression seemed clear

Fig 34 Case 9 Photograph of the patient at the age of 16 years He had always been underdeveloped and was 3 years behind in his studies He complained of headache and sleepiness most of the time, 1 year previously his vision began to fail There were convolutional atrophy, a shadow of a calcified tumor and complete atrophy of the dorsum sellæ, and the floor of the sella was markedly depressed There was bitemporal hemianopsia Vision in the right eye was 6/60, in the left, 6/30 The pathological diagnosis was adamantinoma of the craniopharyngeal duct

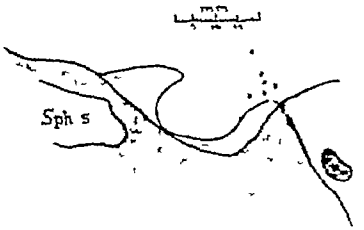

Fig 35 Case 9 A sketch of the roentgenogram drawn to scale showing areas of calcification and enlargement of the sella turcica

Fig 36 Case 9 Photograph of hypophyseal stalk tumor extending from the frontal lobe to the pons

enamel organ The latter is a common observation The basilar layer, spoken of as the layer of ameloblasts, has a well defined basement membrane, above which lie columnar cells with oval, elongated nuclei of a vesicular nature, and with poorly defined cytoplasm Unlike the ameloblasts in the enamel organ these cells are often not in a single layer but tend to assume a more or less stratified formation The distinction between one cell and another in this layer is not sharp because the cytoplasm of one cell seems to blend imperceptibly with that of another Above this ameloblastic layer there sometimes lies a layer two or three cells thick, which is at right angles to the ameloblasts These cells have properties similar to the ameloblasts but they are often lacking in many of the epithelial columns Above them lies the stellate layer, which forms the pulp, so to speak of the epithelial columns These cells when typical appear as stellate cells which form an anastomosing, almost syncytical mass looking very much like primitive mesenchyme They are often not found in this true stellate arrangement, the center of the epithelial column may be composed of cells looking much more like the cells of the stratum interme-

the epithelial portions of the stalk tumors, and from them the stalk tumor has its origin.

These epithelial rests have a lower and upper location. From the lower group arise the tumors which though primarily intrasellar may burst through the diaphragma sellæ early in their career and lie chiefly above the sella. In this lower group of tumors, the sella is enlarged often to a marked degree and the hypophysis compressed or completely destroyed The sellar destruction is caused partly by the fact that the tumor is primarily intrasellar and grows first within the sellar boundaries and partly also by the suprasellar extension This attains large dimensions and destroys the sellar walls by pressure

Tumors arising from the upper group of cells, those just beneath the third ventricle are entirely suprasellar At times they grow into this ventricle and block the outlet of the lateral ventricle. If the tumor be large enough, the sella, and the hypophysis too may be entirely destroyed

Lying above the sella turcica as these tumors do they encroach upon the chiasm and optic nerves. The chiasm is stretched over the tumor and often flattened out, so too the optic nerves if the tumor be of large dimensions.

The position of the tumor in relation to the optic chiasm is important. It may lie below the chiasm, the latter straddling the tumor and present just in front of the chiasm Or lying behind the chiasm it may push the latter forward and make the tumor inaccessible

These tumors vary a great deal in size some are small others very large. One of my tumors was a small lesion covering the floor of the third ventricle another was so large that projecting forward between both frontal lobes, it compressed the anterior and middle cerebral arteries and caused softening in their distribution Many of these tumors are retrochiasmal they grow backward rather than forward and occupy the base of the brain from the chiasmal region to the pons. Whether large or small they are almost always so adherent to the structures at the base of the brain and to the hypothalamus that it is well nigh impossible to enucleate them without serious injury to these important structures The stalk tumors are discrete lesions well encapsulated, but because of their attachment to adjacent structures they must be looked upon as malignant rather than benign This attachment is not due to invasion of the base of the brain by the tumor but to firm adhesions. The capsule of the tumor is adherent to the basilar structures at many points and so firmly attached that it is impossible with any degree of safety to separate the tumor from the adjacent structures.

Not only may these tumors grow forward into the anterior fossa but they not infrequently grow upward into the third ventricle. Thus arise signs of increased intracranial pressure and hypothalamic involvement.

The tumors in question are partly cystic and partly solid. The cystic portion varies greatly in size. In some tumors it may constitute three-fourths or seven-eighths of the tumor in others it is much less extensive Of the solid portion much is often calcified or even ossified. In one case in my series the tumor was so extensively calcified that it was most difficult to obtain a piece for sectioning Much of the solid portion is often necrotic. Usually these tumors have thick firm tough capsules so that even though the cyst be evacuated the cyst wall may not collapse.

The microscopic structure of these tumors is quite constant They consist of a solid epithelial tree with branching and anastomosing offshoots (Fig 42) They are composed of epithelial columns which intertwine and anastomose forming a complicated and often confusing network of columns among which is a more or less abundant stroma The amount of the epithelial structure varies a good deal with different tumors in some it is abundant in others scarce and the caliber of the column varies from a very thin cord-like structure to very plump epithelial growths.

The tumors are said to resemble the embryonic enamel organ and typical sections from the epithelial tree show a basilar layer of columnar cells a stratum intermedium and a stellate layer Often, however these three layers are not seen in the epithelial columns. Either the stratum intermedium is missing, or the stellate layer lacks the absolutely characteristic appearance that it possesses in the

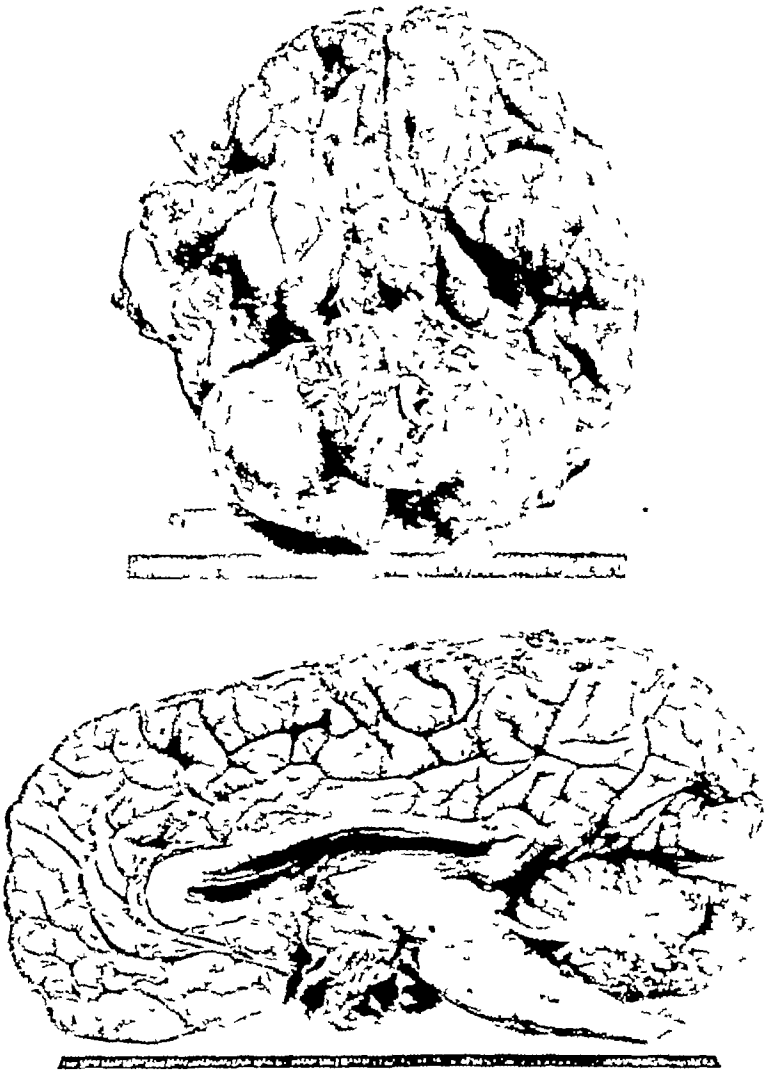

Fig 39 Case 11 At autopsy a large tumor was found at the base of the brain with all the characteristics of a stalk tumor

An important feature of the epithelial columns is the epithelial nests composed of concentrically arranged cells in the columns These are extremely abundant in some tumors and in others are a rather unimportant feature Similar cell collections are sometimes found near the developing tooth in man though their significance is not clearly understood Keratinization has been found in some of these cells, but Erdheim denied the presence of keratin granules

Giant cells have been described in these tumors but we have not seen them even in areas in which degeneration has been very active Similarly glial cells are said to be present in the stroma, but in a careful survey of our tumors we have failed to find any

One interesting feature deserves further attention The similarity of these stalk tumors or adamantinomas to the embryonic enamel organ has often been mentioned In some instances the similarity is striking and in others

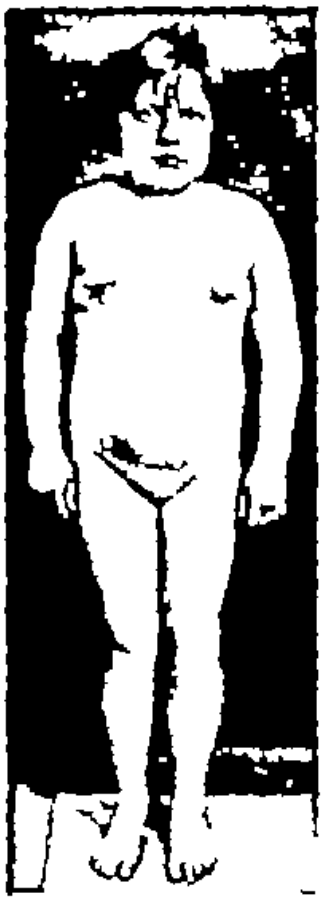

Fig 37 Case Photograph of a girl 8 years of age with signs of intracranial pressure, atrophy of dorsum sella, headaches vomiting, choked disc, arrest of growth, and adiposity

Fig 38 Case 1 A sketch of the roentgenogram drawn to scale Atrophy of dorsum sella, complete disappearance of posterior clinoid processes No calcification

dium The nuclei in the cells of the stellate layer are vesicular and oval and cytoplasmic bridges are sometimes seen

The stroma of these tumors varies in its abundance in some plentiful and in others scanty In some portions it has a distinctly fibrillar nature in others it has a myxomatous appearance and in still others it is almost completely degenerated The number of cells within the stroma varies widely but on the whole cells are not very numerous within it Many of the cells are of a fibroblastic nature Often polynuclear cells are found within its meshes large vacuolated cells are often seen

Evidences of degeneration constitute one of the most constant and interesting features of stalk tumors Cysts are present in most of the tumors sometimes in great abundance in others in small numbers, but in some so cystic that they appear to be a conglomeration of cysts lying among epithelial columns The cysts may be very small or may be so large as to fill almost an entire low power field they are usually filled with a homogeneous, pink staining colloid-like material Within the stellate layer are often large swollen round cells with very small nuclei and with vacuolated cytoplasm These cells probably represent cells of the stellate layer that have undergone hydropic degeneration

In most of these stalk tumors groups of stellate cells may be seen with hyaline degeneration they are usually compressed take a homogeneous pink stain and appear to be definitely degenerated In some of them small granules of calcium are present and it is possible that they may undergo calcification eventually One of our tumors had a tremendous number of these areas In a few tumors one could see the beginning of this degenerative process in the epithelial nests so often seen in the epithelial columns and it may be that these nests may eventually undergo degeneration of the sort described

Calcification is seen in almost all the tumors and so abundantly that it may appear in every field (Fig 43) The calcified areas may be seen as frequently in the stroma as in the epithelial columns, though probably more abundant in the former It appears as small calcified granules, as a conglomeration of granules, as small flat sheets of calcified material or as large irregular calcified masses Bone formation is said to occur in some parts of the tumor but we have not observed it in any tumor of our series

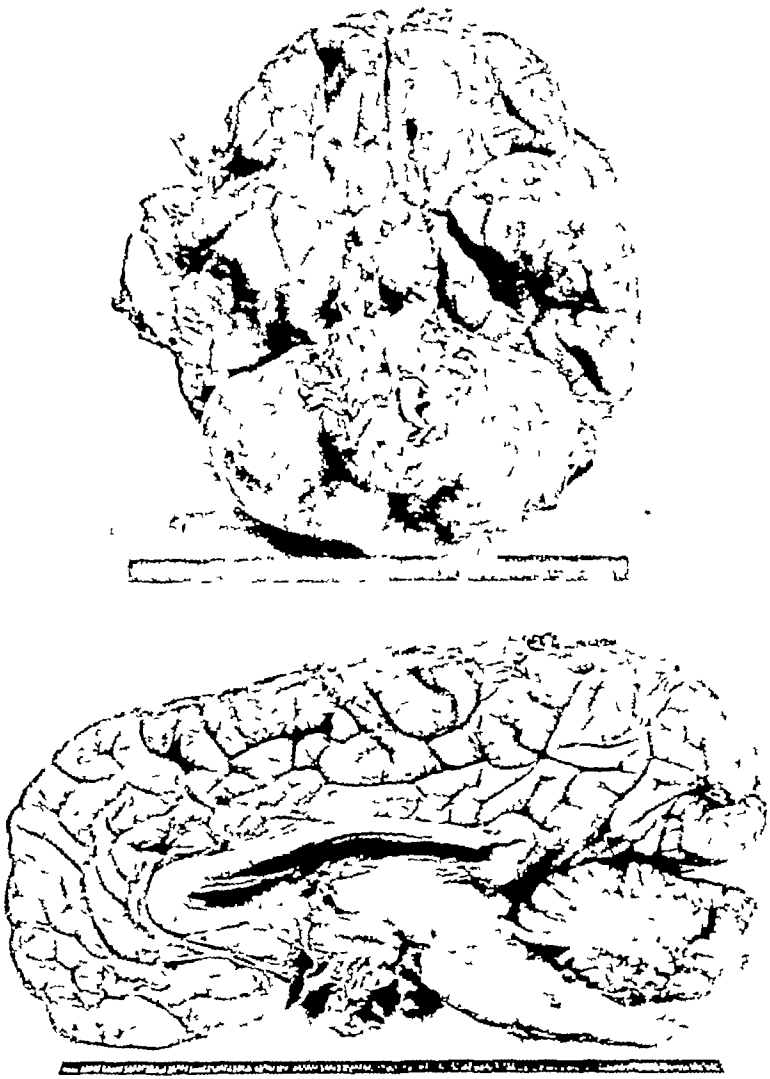

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Fig. 40. Case 1. A sketch of the roentgenogram drawn to scale. No enlargement of sella turcica. No calcification.

Fig. 4. Case 2. Hypophyseal duct tumor. Photograph of patient 8 years after operation.

much less so. In a general way they resemble the enamel organ but it is strange that in none of the tumors described has enamel been found. The ameloblasts of the tumors contain no granules within their cytoplasm and the tumor itself possesses no structure that can be said to resemble enamel even remotely.

When discussing the origin of these tumors, we are confronted with a difficult problem. Presumably they arise from those remnants of the hypophyseal stalk that have been carried along the anterior lobe of the hypophysis in its evolution and development. In their structure the stalk tumors resemble adamantinomas and for this reason have been so called. But because the basilar layer of cells resembles the ameloblasts, it has been proposed by Ivy and Churchill that these tumors be called ameloblastomas. While it may be conceded that the hypophyseal stalk is composed of a stratified epithelium, no one has demonstrated that the type of epithelium in the stalk and the type seen in these tumors is identical. The stalk remnants are composed of stratified squamous epithelium, the epithelial portion of the stalk tumors, while epithelial in nature, is not squamous and has a structure quite distinctive. Certainly the ameloblast like cells in the basilar layer are not to be found in the stalk remnants. Carmichael attempted to demonstrate the histological similarity of the stalk remnants and the stalk tumors, but a study of his sections fails to reveal a close resemblance. The tumor structures are epithelial in nature but not squamous in type.

We have therefore the following situation: the hypophyseal duct in the embryo is lined with a low cuboidal epithelium according to Carmichael and with a modified squamous epithelium according to Duffy. The stalk remnants are composed of a stratified squamous epithelium of a special type unlike that of the stalk or its remnants. How can one explain the discrepancy and maintain the thesis that these tumors originate from the stalk? The paradox is not as difficult as it seems to appear.

The hypophyseal stalk in the embryo is intimately connected with the buccal cavity. Transition forms of epithelium are numerous in this region: transitions from ciliated columnar epithelium to low cuboidal or even flat cells and even to a modified squamous epithelium may be followed. It is not surprising therefore that the structure of the stalk tumors differs from that of the stalk or its remnants since they may represent only transition stages. It is more difficult to explain the great uniformity in structure of these tumors for they are always alike in their epithelial portions at least. Thus it is difficult to correlate them with tumors that arise from transitional epithelial elements. One would expect a diversity rather than a uniformity of structure. So too it is difficult to disregard the similarity which these stalk tumors bear to the primitive

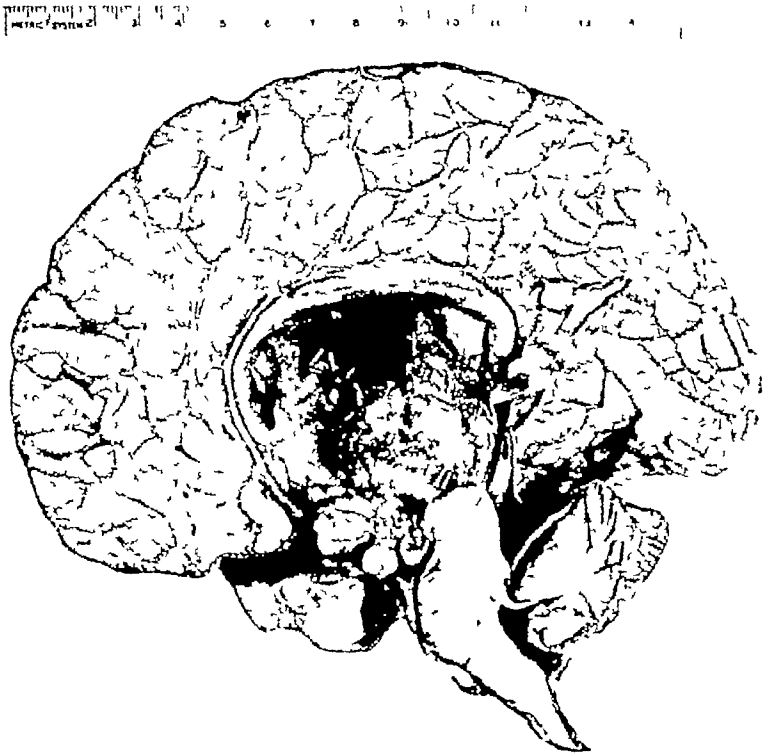

Fig 45 Mixed tumor Suprasellar

The cyst was opened, the cavity was irregular in shape, and contained no tumor tissue No attempt was made to remove the cyst wall and the wound was closed

Readmission February 13, 1923 In the interval, the patient's condition improved The convulsions had ceased only to return July, 1922, and later the signs of intracranial pressure recurred At this time the cyst was again evacuated and 500 cubic centimeters of the same yellowish oily fluid recovered

At this time, when the boy was 11 years old, there were signs of sexual precocity (Fig 47), the sex

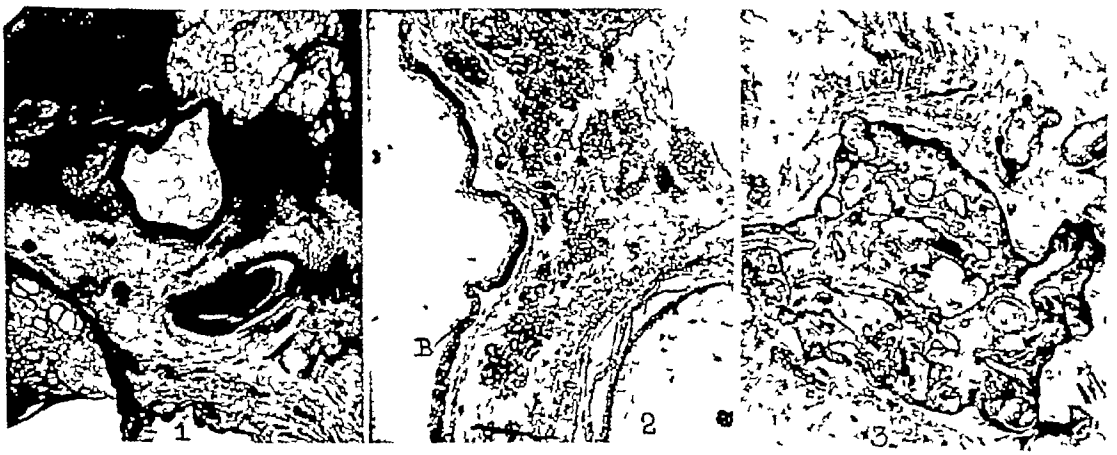

Fig 46 Sections from the same tumor showing left, an area of cartilaginous tissue at *A* fat tissue at *B*, center, an area of glandular tissue at *A* and epithelium at *B*, right, an area of osteoid tissue Hematoxylin and eosin stain

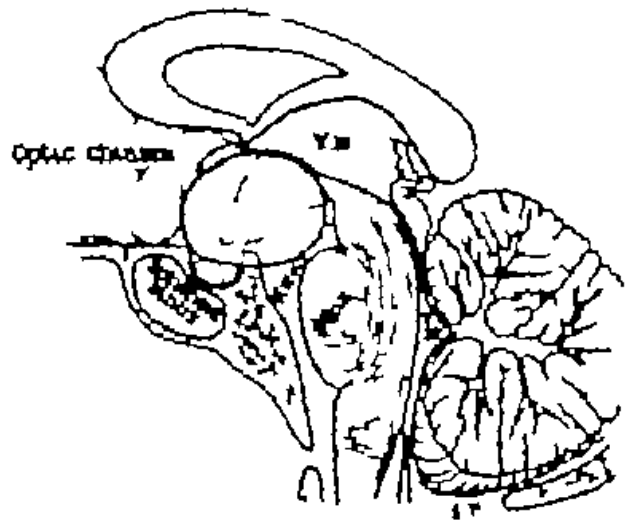

Fig 44 Suprasellar teratoma eroding sella and compressing optic nerves and chiasm It is chiefly retrochiasmal

primary teratoid tumors 8 were in the region of the hypophysis Of 4 teratomas in my series, 2 were suprasellar 1 was in the third ventricle, the fourth in the cerebral hemisphere Both of the suprasellar teratomas occurred in young people 1 a girl, the other a boy both in their ninth year

The relation of these congenital tumors to the structure around the sella differs somewhat from that of the more common stalk tumors (Fig 44) They are chiefly retrochiasmal displacing the optic chiasm upward and forward and sometimes compressing the optic tract As a rule the teratomas extend upward into the third ventricle producing intense hydrocephalus and by virtue of their size may compress adjacent structures and give rise to such neighborhood symptoms. Sometimes the suprasellar portion may simply be an extension from an adjacent intracerebral teratoma

They may be chiefly cystic or chiefly solid The latter portion is usually firm almost hard and may contain extensive calcified portions In one of my cases the gross appearance of the tumor was that of a lipoma In fact probably seven-eighths of the tumor was lipomatous. Only on microscopic examination were the derivatives of the other cell layers discovered and the tumor found to be a teratoma Like the stalk tumors they are so firmly adherent to the structures at the base of the brain that complete extirpation is impossible Like other congenital tumors of the brain, such as the stalk tumors they occur not only in young but in older individuals, as in one of my patients who was in his fortieth year (File No 28738)

Teratomas are usually large tumors, filling the entire interpeduncular space and encroaching upon the mesial aspects of both temporal lobes (Fig 45) They may contain areas of calcification which are sufficient to cast an X-ray shadow Histologically they contain elements of all the germ layers and differ in no way from teratomas elsewhere (Fig 46) Many tumors of this group, however have been classified as teratoid tumors because they contain the derivatives of only some of the germinal layers Typical teratomas in the brain, like those in the testis and elsewhere contain epithelial elements glands bone, fat blood vessels cartilage connective tissue and muscle

Case 13 A child of 9 was under observation at intervals for 6 years The lesion at first presented as a large cyst from which large quantities of an oily yellowish fluid were evacuated on two occasions in the first 2 years Later the cyst was replaced by a calcified tumor which proved to be a teratoma Convulsions, hemiparesis, homonymous hemianopsia, sexual precocity with headache, nausea and vomiting, were the outstanding symptoms The patient died in his fifteenth year

Clinical history A boy E F aged 9 years (File No 63844) was first admitted to the neurosurgical service of the University Hospital June 1 1921 with a chief complaint of convulsions Two years before admission he developed severe headaches and spells of vomiting Six months before admission his mouth was drawn to the right side his gait was unsteady and his memory began to fail His head was increasing in size so that in 2 years the size of his hat changed from a No 6 to a No 7½ There was definite bulging of the right temporal region

Examination revealed an underdeveloped boy with lower left facial paresis, adiadochokinesis and dysmetria left impairment of pain and temperature sense on the left side of his body and face a horizontal nystagmus on turning and past pointing The discs were pale the veins tortuous and there was a subsiding papilledema left eye plus 4 diopters, right eye plus 5 diopters The roentgenogram showed convolutional markings

Operation July 26 1921 Exploratory craniotomy exposing the right motor and temporal cortex. The bulging of the temporal bone suggested an attempt at spontaneous decompression From a cannula introduced into the right temporal lobe 150 cubic centimeters of a yellowish oily fluid escaped

blindness was frequently recorded Whereas in the teratoma patient, though afflicted for at least 8 years, his vision at the time of his death was 6/15 in each eye

There are in the record of this instance of teratoma many other features that might arouse discussion not only as to diagnosis but as to treatment But what has been said suffices to illustrate the essential differences in the physical expression of these two lesions, both as it were of congenital origin, the stalk tumor arising from a remnant of the hypophyseal stalk, the other, the teratoma, from some embryonic rest in the hypophyseal region The origin of these tumors is by no means as clear as in the case of the stalk tumors but it is possible that the suprasellar teratomas arise from remnants of tissue connected with the buccal cavity

(*To be concluded*)

EVACUATION OF THE GALL BLADDER IN OLD AGE[1]

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THE present article is the third of a series of statistical analyses utilizing the Graham-Cole method of visualizing the human gall bladder and dealing with the rate of emptying of the biliary vesicle in different periods of life

In the first study (1928) the technique of computing volumes was refined the various factors that might influence the rate of emptying were tested experimentally and records were made of the entire period of evacuation of the gall bladder in 24 young men and women of medical school age. These observations established the main features of the curve of contraction in human beings and showed that the most important period is the first three quarters of an hour after a test meal by which time an average of two-thirds to three quarters of the contents of the gall bladder has been evacuated depending on the sex.[2]

In the second study (1934) after the data for young adults had been revised and 6 new cases added, observations were extended to 28 boys and girls 6 to 11 years of age. This study revealed a striking difference between the mean rate of evacuation in the two groups 80 per cent of bile being discharged in children as against 69 per cent in young adults during the first 40 minutes after the test meal When analyzed according to sex however this difference between children and adults was found to be due almost entirely to the faster emptying of the male since the gall bladder of the girl seems to remain constant in its rate of discharge while passing from childhood to young womanhood.[3]

MATERIAL AND METHODS

The present study deals with the evacuation of the gall bladder in a group of 24 men and women between 60 and 78 years of age (average 66 years) All of them were patients in the University Hospital who volunteered to submit to this test at no little inconvenience and discomfort to themselves.[4]

The procedure employed was similar to that used in the preceding studies Having ascertained that the patient had a negative gastro-intestinal history 3 5 grams of iodeikon was administered orally during the evening The next morning before breakfast the patient was roentgenographed at 2 4 8 12 16 20 25 30 35 40 and 45 minutes after drinking a glass of four egg yolks mixed with an equal amount of milk and seasoned with sugar Exact tracings of the cholecystograms were then made and the changing volumes of the gall bladder computed in cubic centimeters according to the methods described in the 1928 and 1934 articles. Subsequently a contraction curve for each patient was obtained by plotting these volumes against time (Fig 1) Finally in order to secure a curve of the mean rate of emptying for each sex and for the whole group the percentage loss of volume was calculated for each 8 12 20 30 and 40 minute reading (Table I) and the reciprocals of the sums plotted against time In this as in the previous study the 2 minute reading has been considered as unity (unless otherwise noted) that being the earliest reading at which the slack in the gall-bladder wall is taken up by contraction

[1] The test meal used in the first series was the original Boyden meal (1928) consisting of five egg yolks well stirred in half pint of cream In the series dealing with children, the dosage was cut to three egg yolks diluted in milk and sweetened with sugar In the more recent work the "meal" for adults has been standardized at four egg yolks mixed with an equal amount of milk and sweetened with sugar If it is necessary to disguise the egg taste, little sherry flavoring or vanilla may be added The essential ingredient of this meal is egg yolk, no other natural food comparing with it as a stimulus of emptying the gall bladder (See discussion, p 11 cited article) This original observation has been verified by numerous investigators and particularly by Brunner (1928), an outstanding experimentalist in this field in Germany Brunner uses egg yolk alone, but the writer still favors the addition of milk or cream, partly to make the yolk more palatable

Since this article was written the writer has encountered three brief references to the emptying of the gall bladder in children Weber (1927) seems to have been the first to consider the problem While he was concerned chiefly with methods of visualization, his account contains two cholecystograms I an 8 year old boy that demonstrates an excretion of about half the contents of the gall bladder within 30 minutes after "meal rich in fat" Brennan (1930) observed the rate of emptying in 10 cases, the youngest of which was 3 years old Without giving any details, he states that he was able to demonstrate very extensive emptying in 12 to 24 hours and that evacuation in children as contrasted with that of old people, is characterized by the very reduced amount of bile left in the gall bladder an hour and half after meal of egg yolk Finally Monsarrat-Augustin (1934) makes the statement, in his interesting book on the radiology of the biliary vesicle, that it takes less time to empty the normal gall bladder of the child (p 3)

[4] The authors are also indebted to Dr O H Wangensteen, chief of the Surgical Service, and to Dr L O Rigler, head of the Department of Radiology for supplying hospital facilities for carrying on this work

From the departments of Anatomy and Surgery The University of Minnesota, aided by grant from the medical research funds of the Graduate School.

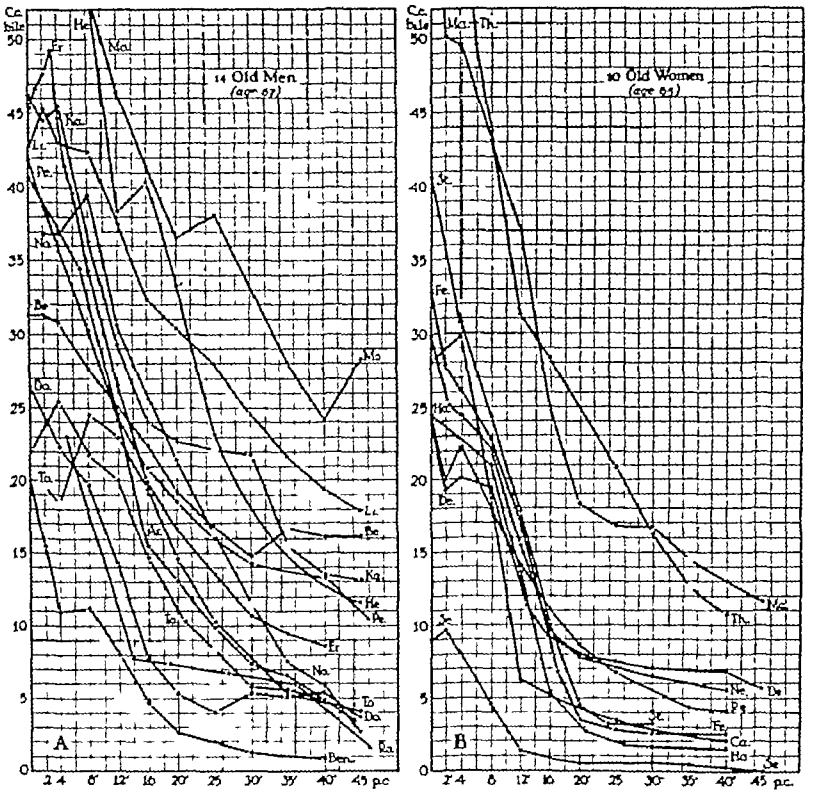

Fig 1 Individual contraction curves of 24 *old* adults, covering the first phase of evacuation of the gall bladder Ordinates, cubic centimeters of bile in fundus, body (and infundibulum) of gall bladder, abscissas, minutes post cibum (after a meal of four egg-yolks and milk), *Er*, *He*, *Mo*, etc., names of patients See corresponding abbreviations in first column of Table I for original data.

RATE OF EMPTYING IN SEVENTH DECADE

When the assembled contraction curves of old and young adults are compared (Figs 1 and 2), no outstanding differences are apparent although it may be noted that the curves for the older group are somewhat steeper and more regular, also that larger gall bladders are more frequent there than in the younger group The latter observation is in accord, perhaps, with Luetkens' statement that the biliary vesicle tends to become ptosed and overdistended in old age Furthermore, the older women exhibit a rather surprising uniformity (Fig 1 B), most of the curves of contraction tending to run closely parallel A similar conservative tendency has been observed in young girls (see Fig 7, ref 3) but it has not been observed particularly in young women (Fig 2 B)

These observations, however, are more or less incidental, the principal value of the graphs being to give some idea of the extent of individual variations A true appraisal of the rate of emptying may be obtained only by examining the mean percentage loss of volume for the whole group When this is plotted as a graph (Fig 4 B, solid line), the curve for old people takes up a position intermediate between the curve for young adults and that for children (see also Fig 3 A and B) In other words, the gall bladder of the seventh decade seems to be emptying faster than that of the third decade Yet, when the data for the two groups are submitted to statistical analysis (Table II), it appears that the differences are doubtfully significant, for only in the 40 minute readings are the differences between the means equal to twice the standard error

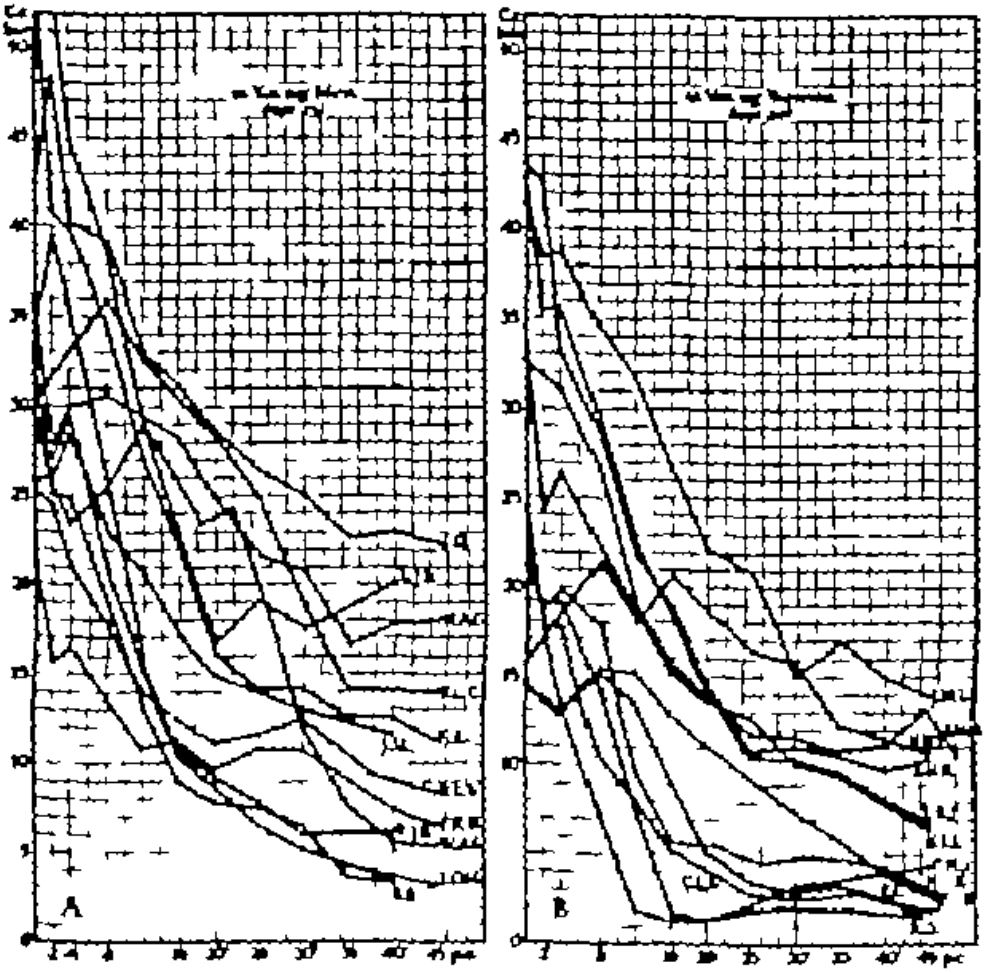

Fig. Individual contraction curves of 24 young adults, covering the first phase of evacuation of the gall bladder following a meal of five egg yolks and cream (see footnote). For original data, see Table III, Boyden and Fuller 1934. For mean rate of emptying according to sex, see Figure 5 B. For methods of computing closures of gall bladder see Boyden, 1928.

That is, the probability (P×100) that the differences might be due to random sampling is as great as 4.5 times in a hundred.[1]

Nevertheless, since the differences between the mean rate of emptying in old age and that in childhood are likewise without significance even though the child gall bladder empties significantly faster than that of the young adult (1934 article)—it is necessary to consider the possibility that the motility of the adult gall bladder increases with age. If this be true, then it must be due either to progressive hypertrophy of the gall-bladder musculature or to a lessening of resistance at the duodenal end of the common bile duct.

[1] In ordinary statistical parlance, if a difference occurs less than five times in a hundred it is assumed that it is not due to chance. The writers are greatly indebted to Dr. Edith Boyd for supervising the statistical analyses in this article.

What evidence exists, however, is conflicting. Thus Luetkens (1926) was unable to substantiate Charcot's claim that the gall-bladder musculature atrophies in old age. More often he received the opposite impression, namely of a slight hypertrophy of individual muscle fibers and so of the whole tunic. But he did note a sagging and distention of the lower end of the gall bladder in old age, which seemed to be associated with a weakening of the elastic fibers. Also in some cases he observed atrophy of the mucosa and sclerosis of the blood vessels. On this basis Nemours-Auguste, 1934, assumes a lengthening of the time of evacuation in old age.

Nor have the authors found any evidence that suggests a progressive weakening of the duodenal or choledochal musculature. Accordingly it seems less probable that the gall

TABLE I—EMPTYING OF GALL BLADDER IN OLD ADULTS

A 10 old women	Age	Weight pounds	Cause of hospitalization	Volume at intervals after eating										
				2 minutes* c cm	5 minutes		12 minutes		20 minutes		30 minutes		40 minutes	
					c cm	Per cent loss	c.cm	Per cent loss	c cm	Per cent loss	c.cm	Per cent loss	c cm	Per cent loss
Re	62	115	Carcinoma, breast	19 5	15 0	9 25	13 0	30 00	8 0	57 00	5 4	75 87	4 2	79 04
Ca	62	141	Carcinoma, breast	28 1 (0 min)	18 7	11 18	6 3	77 50	4 2	85 10	3 0	89 74	2 1	92 60
Ne.	61	125	Carcinoma mouth	24 4 (4 min)	22 2	9 18	15 5	36 40	7.8	67 87	6 6	73 12	5 5	77 38
Ma	60	103	Pernicious anemia	50 1	43 7	1 85	37 0	26 26	18.4	63 29	16 6	66 96	13 0	74 14
St.	78	148	Cataract	30 7 (4 min.)	24 5	0 80	17 8	42 19	4 5	85.42	3 2	89 58	5 9	89 58
Fe	70	115	Lacerated pelvic floor	27.8	9 4	19 54	17 7	36 50	3 5	87.36	2 6	90 52	2 5	91 10
Th.	64	123	Carcinoma, cervix	35 1 (5 min)	43 7	22 10	31 3	44 21	25 0	55.44	16 3	70 95	10.8	80 75
Se	66	105	Hydrometrahidis	9 0 (0 min.)	4 5	50 44	1.4	84 06	0 5	94 69	0 5	94 69	0 24	97 35
Ha.	55	125	Carcinoma, uterus	24 4 (0 min)	21 1	13.45	13 6	44 26	3 8	84 26	1 7	93 12	1 5	93 77
Ro.	69	103	Lacrimal fistula	19 5	19 5	00 00	13.0	33 30	8 1	57 69	7 0	63 50	6 8	64 75
	165 2	1119 8		120 0		190 97		454 97		738 21		808 05		810 46
Mean percentage loss in 10 old women						19 10		45.47		73 82		80 8		84 05
B 14 old men														
Ro	61	150	Carcinoma tongue	23 0 (5 min.)	18 0	21 60	11 2	51 2	7 2	68 64	6 6	74 20	4-4	80.84
Be	70	155	Carcinoma mouth	32 8 (4 min)	27 7	10 00	15 0	18 70	19 2	37 66	14 8	51 95	16 0	51 95
Ka.	70	173	Carcinoma lips	44 5	36 3	18.43	29 3	34 16	22 8	48 76	21 8	51 00	13 5	68 06
Ta.	69	150	Carcinoma ear	22 0 (0 min)	21 8	1 09	20 5	7 64	11.4	48 37	5 8	73.82	3 9	82 18
Mo	73	150	Carcinoma, rectum	48 6 (0 min)	(52 7)	0 00	46 1	4 74	36 6	24 69	33 0	32 10	24 1	50.41
He.	67	120	Pulmonary tuberculosis	45 5	(54 2)	0 00	37.4	17 89	33 3	26 86	27 8	68 83	12 6	72 30
Do	72	109	Carcinoma mouth	22 3 (4 min)	19 7	11 85	14.0	37 28	5 3	76 35	4 1	81 72	4 1	81 72
Ar	72	134	Trifacial neuralgia	34.4 (7 min)	32.0	6 98	24 5	28 78	23 1	71 92	7.4	78 49	4.8	86 05
To	61	164	Carcinoma, tongue	28.4 (4 min)	(24.4)	0 00	(23 5)	0 00	14 5	21 20	7 7	58 16	4 7	74.46
Ben	61	164	Carcinoma esophagus	25 5	11 2	27 75	8 1	47.87	2 5	84 00	1 3	91 74	0 9	94 33
Ir	72	120	Chronic inflammation of forehead	42.9 (0 min)	42 4	1 17	37 6	12 35	30 3	24.48	24 4	43 12	19 4	54 76
Pe	60	137	Carcinoma prostate	38 7	30 2	21.96	24 2	37.47	18 5	52 70	14 2	63 31	13 6	64 86
No	63	146	Aortic insufficiency	36 0	39 5	0 00	30 6	17 14	21.4	42 08	11 5	68 76	5.9	83 95
Er	63	171	Secondary anemia	44 7 (0 min)	34 3	23 26	26 6	40.61	16 6	62 79	10 6	76 21	8 6	80 65
	166 7	1145 7		133.4		144.07		355 85		690.00		913 55		1037 15
Mean percentage loss in 14 old men						10 20		25.42		49 29		65.25		71 27
Mean percentage loss in 24 old adults						13 96		33 77		59 51		72 73		77.82

*Considered as 100 per cent substitute readings are noted in parenthesis.
†Average

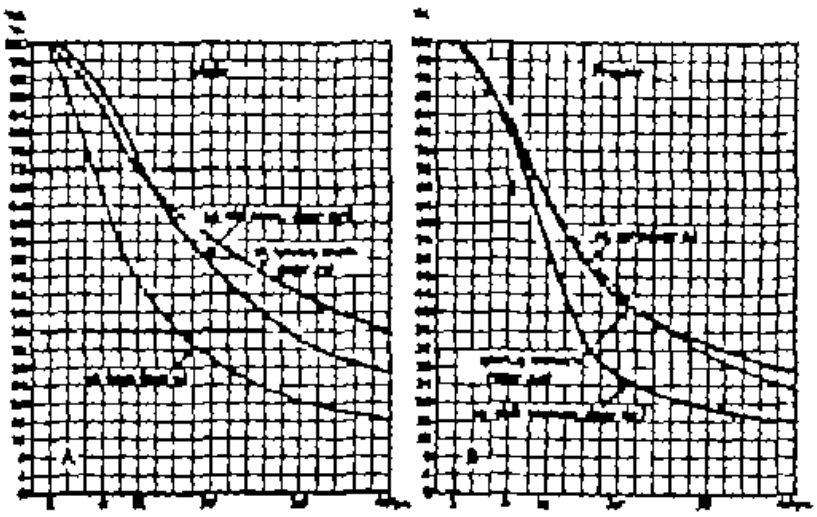

Fig. 3. Graphs illustrating the mean rate of evacuation of the gall bladder in childhood, early maturity and old age arranged for comparison of age differences in the same sex. A, Male, B female. Ordinates, percentage of bile in gall bladder, based on the two minute reading (see 5th column, Table I). Abscissa, minutes post cibum.

bladder empties faster in old age than that our samples of the older population are not representative of the old age group. In other words, it is quite likely that the curve for old age shown in Figure 4 B represents the reaction of the more favored members of a hospital group—namely those who have escaped infection or obstruction of the biliary tract. For when we examine the total number of patients subjected to these tests it is apparent that more individuals in the old age group had to be eliminated on account of non visualization of the gall bladder than in either of the other age groups (see last column, Table III). In the medical students for instance *100 per cent of all gall bladders tested* by the Graham-Cole method were visualized. In the hospital children at least 86 per cent could be seen but in the oldest group only 74 per cent were visualized. Furthermore in comparing the series that were discarded because of obliterating accumulations of gas and stools one should bear in mind that the 8 children grouped in the third line and column of Table III are much less likely to have been pathological than the 5 old people in the fifth column, for it is well known that air is swallowed in much larger amounts by children than by adults.

A survey of the three groups thus leads to the conclusion that the medical student group is the most representative one, that the children come next and the old age group last. Accordingly it is believed that the most that can be concluded from the mean curve of emptying in the seventh decade is that if the biliary tract escapes pathological alteration its power of evacuation will not lessen with age.

Apparently the only other investigator to subject the matter to experiment has come to similar conclusions. Thus Brouner (1929) who investigated 6 patients between the age of 60 and 70 years—each with a negative stomach and gall-bladder history—found that up to the first 90 minutes after ingestion of egg yolk the motility of these gall bladders seemed *in no way to have been retarded*. This convinced him that their musculature was in no way insufficient. On the other hand, he observed that there was a much greater residue of bile in the gall bladders of 6 older patients (90 minutes after egg yolk) than in 10 young children whom he examined. He estimated that it ranged from 1/10 to 1/2 the ante-cibal volume—an average residue of 25 per cent—which is more than twice as much as the writer found in 24 young adults (see Table III, 1928). Although Brouner's cases were few in number and his estimates were merely guesses, it is possible that the later and least important places of contraction in old age undergo retardation or curtailment.

TABLE II—STATISTICAL ANALYSES

Time interval min	Cases	Mean and standard error	Cases	Mean and standard error	Difference and standard error	Difference standard error	Probability integral
A. Old adults vs. Young adults							
8	24	13 96±2 585	24	15 75±3 134	−1 79±4.063	441	0 660
12	24	33 77±4 125	24	31 33±4.839	+2 44±6 359	384	0 704
20	24	50 51±4 513	24	50 08±5 566	+9 43±7 166	1.316	0 186
30	24	71 73±3 341	24	61.06±4 600	+10 67±5 685	1 877	0.060
40	24	77.82±2 701	24	68.87±3 530	+8 95±4.445	2 013	0.045
B Old men vs Old women							
8	14	10 29±2 782	10	19 10±4 505	−8.81±5 295	1 664	0 098
12	14	25.42±4 386	10	45 47±6 270	−20 05±7 653	2 620	0 009
20	14	49 29±5 601	10	73 82±4 738	−24 53±7 336	3 344	0.001
30	14	65 25±4 372	10	80 81±3 741	−15 56±5 704	2 704	0.007
40	14	73 37±3 626	10	84 05±3 282	−10 68±4 891	2 184	0.030
C Adult men vs Adult women							
8	26	12 12±2 157	22	18 08±3 514	−5 96±4 123	1.446	0 147
12	26	26 59±3 501	22	39 59±5 184	−13 00±6 255	2 078	0 038
20	26	46 62±4 562	22	64.46±5 114	−17.84±6 853	2 603	0 009
30	26	60 83±3 507	22	72 97±4 525	−12 14±5 725	2 121	0.034
40	26	69 30±3 024	22	78 13±3 284	−8.83±4.464	1 978	0 048

SEX DIFFERENCES IN RATE OF EMPTYING

The mean rate of evacuation in the three age groups according to sex is indicated in Figure 5 In the 1934 article, it was shown that the more rapid emptying of the biliary vesicle in boys than in girls (Fig 5 A) was statistically significant But it could not be demonstrated statistically that the gall bladder of young women emptied faster than that of young men It was believed, however, that the consistent differences between the two curves (Fig 5 B) indicated that larger samples would probably show a sex difference in favor of the female Thus it was pointed out that 6 additional cases in men revealed a similar slowness of emptying [1] Also it had been shown in the 1928 article that it took nearly twice as long to empty all but 3 cubic centimeters of the contents of the gall bladder in 12 young men as it did in 12 young women—namely, 128 as against 68 minutes (Table III)

We were not surprised, therefore, when statistical analysis of the curves for old age (Fig 5 C) showed that the rate of emptying for the older women was significantly faster than that for the older men For, as indicated in Table II B, the probability that such differences might be due to random sampling is less than 1 100 during the period when the gall bladder is emptying the fastest (12 to 30 minutes after meals) Similarly, when the data for young and old adults are combined, statistical analysis again decides in favor of the female (Table II C)

The evidence in these three studies, therefore, points to a sex difference in all periods of life Before puberty, the male gall bladder empties much faster than the female, after puberty it slows down to a rate that is distinctly inferior to that of the female which has pursued a constant tempo from childhood to old age

Two questions at once arise What is the meaning of this change in the tempo of the male and how can this conservatism of the female gall bladder be reconciled with its greater susceptibility to biliary disease? We would approach the problem by suggesting

[1] As these earliest cases had been roentgenographed at 15 minute intervals, the data could not be fitted to that in the table, since the latter was based on shorter intervals

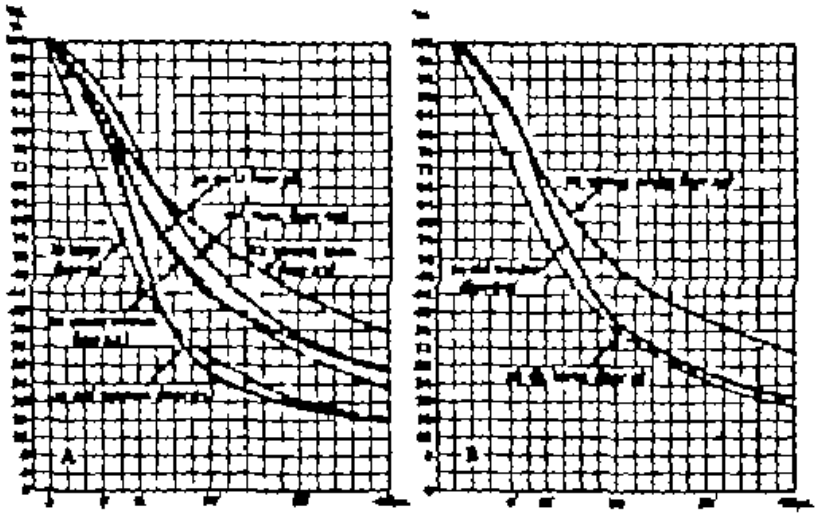

Fig. 4. Assembly diagrams illustrating the mean rate of evacuation of the gall bladder. A, five groups divided according to age and sex. B, three groups divided according to age alone.

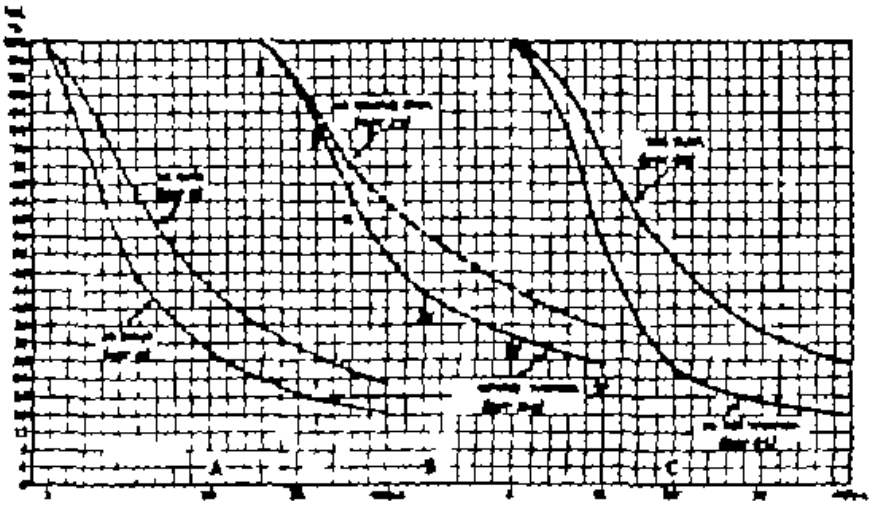

Fig. 5. The three age groups arranged for comparison of sex differences.

that the issue is not so much concerned with the gall bladder as with the intestinal tract, for the work of the last decade—particularly Ivy's notable demonstration of the existence of a duodenal hormone that specifically activates the gall-bladder musculature—makes it clear that, from the standpoint of motility the human gall bladder is nothing but a puppet whose strings are being pulled by a chemical robot strategically placed in the upper half of the small intestine. It is believed therefore that sex differences in the rate of discharge of the gall bladder must be sought for in changes that occur during the prepubertal growth of the gastro intestinal tract. It is not inconceivable for instance, that the prime mover is the hypophysis and that the changes may be of the sort that Clark (1935) has recently described for the testis, in her demonstration of a prepubertal reversal of sex difference in the gonadotropic hormone content of the pituitary gland.

Similarly the greater susceptibility of the female gall bladder to disease is now generally attributed to metabolic disturbances or to changes in the mucous membrane of the gall bladder following infection or obstruction of the duct system (cf. Ravdin 1934) rather than to stasis caused by lack of motility of the gall bladder. Indeed, it appears that the human gall bladder is not even subject to inhibitory reflexes arising from painful stimulation of stomach and duodenum (Boyden and Rigler 1934)—reflexes which in certain lab-

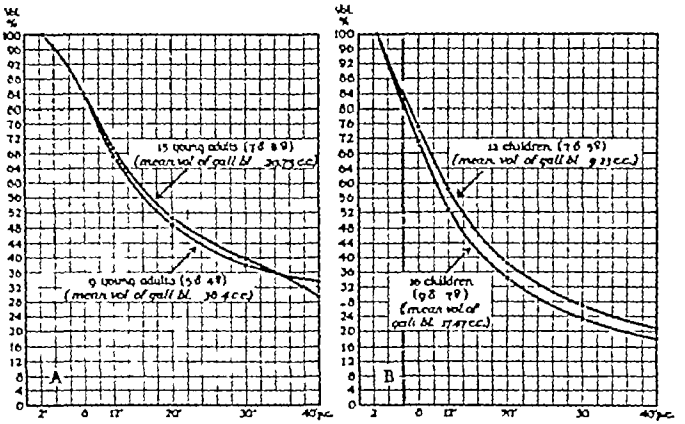

Fig 6 Graphs illustrating the negative effect of size upon the rate of evacuation of the gall bladder A, In young adults, B, in children

oratory animals, retard the contraction of a gall bladder that is emptying after a meal of egg yolk (Oughterson and Mendillo, 1933, Birch and Boyden, 1930) Loss of motility in the human gall bladder is thus to be interpreted as a consequence and not as a cause of biliary tract disease

THE EFFECT OF GALL-BLADDER SIZE ON THE RATE OF EMPTYING

Since it is assumed that in adults the female gall bladder is generally smaller than the male —and our data lend support to this view—it has seemed desirable to inquire whether the faster rate of emptying in the female is a function of its size Accordingly, the data compiled from students of medical school age have been arranged in two categories—gall bladders having an initial volume of over 30 cubic centimeters and those having less

When the mean curves of emptying for these two groups are compared (Fig 6 A), the small gall bladders (having an average content of 20 75 cubic centimeters and a sex ratio of 47 per cent males) show approximately the same rate of contraction as the larger ones (averaging 38 4 cubic centimeters and having a sex ratio 55 per cent males) Obviously, in this group, size is not a significant factor

Similarly, the children have been divided into two groups—those with gall bladders having an initial volume above 12 cubic centimeters (an average content of 17 47 cubic centimeters, with a sex ratio of 56 per cent males), and those below 12 cubic centimeters (averaging 9 23 cubic centimeters, and with a sex ratio of 58 per cent males) Here, also, there is no appreciable difference If any-

TABLE III —SUMMARY OF CASES IN THREE AGE GROUPS

	Young adults (students or younger members of laboratory staff)		Children (patients in University Hospital)		Old people (patients in University Hospital)	
	No	Per cent	No	Per cent	No	Per cent
Number tested by dye	34		42		39	
Male	22	65	22	52	23	59
Female	12	35	20	48	16	41
Number well visualized	30*	94	28	67	24	62
Male	20	91	16	73	14	61
Female	12	100	12	60	10	63
Number insufficiently visualized for computation of volumes	2	6	8	19	5	13
Male	2	9	3	14	4	17
Female			5	25	1	6
Number not visualized			6†	14	10‡	26
Male			3	14	5	22
Female			3	15	5	31

Percentages are given in round numbers (hence, occasionally, they add up to 101 per cent)

*Two of these gall bladders (males) failed to empty after standard meal, therefore only 30 cases (88 per cent) could be used for plotting contraction curves The first 6 males (Harvard series recorded in 1928 article) were omitted from the 1934 article, since those cholecystograms had been taken at only 15 minute intervals. Six new cases (Minnesota series) were substituted The remaining 18 series were made at the University of Illinois.

†It is not known whether these cases were visualized, since the gall bladder region was completely obscured by gas or stools. The percentage of children with normal gall bladders ranges therefore from 80 per cent upward

‡None of these cases was visualized, although the gall bladder region was not particularly obscured by gas Only 74 per cent of old people were visualized therefore

thing the smaller gall bladders empty slower *but not significantly so (Fig. 6 B)*

Unfortunately the old age group could not be separated successfully into two categories since in the group which exceeded 30 cubic centimeters in volume (an average of 42 cubic centimeters for 12 subjects) the males out numbered the females 3 to 1 This was true also of the combined figures for young and old adults for in gall bladders over 30 cubic centimeters (an average of 35 7 cubic centimeters for 21 adults) the males outnumbered the *females 2 to 1 (Below the 30 cubic centimeters level an average of 20 9 cubic centimeters for 27 adults—the males constituted only 44 per cent)* The figures for children and young adults, however afford no evidence that size is a factor in the rate of evacuation of the gall bladder

CONCLUSIONS

This article presents a comparative study of the rate of emptying of the biliary vesicle *in three periods of life* childhood early maturity and old age

It is based upon cholecystographic examination of 115 individuals ranging from 6 to 78 years of age 84 of whom were well enough visualized to permit computation of gall bladder volumes at frequent intervals after a meal of egg yolk

Statistical analysis of this material indicates that the mean rate of evacuation of the gall bladder is faster in childhood than in early maturity the difference being wholly due to the faster rate of emptying in boys

After puberty the male gall bladder reverses its position becoming significantly slower than the female

Old adults in our series appear to evacuate the gall bladder faster than young adults but in view of the fact that only 74 per cent of the gall bladders of older people could be visualized as compared with 100 per cent of the young adults it is believed that the old age group from which we obtained our figures represents a selected sample of the population — a group that has escaped biliary disturbances Accordingly these results are interpreted to mean that if the biliary tract escapes *pathological alteration its motility* does not become impaired by old age

Old women have a much higher rate of emptying than old men—81 per cent of the contents of the female gall bladder being evacuated 30 minutes after a meal of egg yolk as compared with 65 per cent in the case of the male gall bladder

These observations support the view that the greater susceptibility of women to gall bladder disease is due to such factors as liver *dysfunction metabolic disturbances impairment of* the absorptive functions of the gall bladder etc. rather than to any constitutional inferiority in the rate of evacuation of the biliary vesicle

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CHOLECYSTITIS WITH CHOLELITHIASIS

A Clinicopathological Study of Sixty Patients

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THE purpose of this study was to reinvestigate the correlations between the clinical manifestations of cholecystitis and cholelithiasis, and the morphological changes in the gall bladder and its content In order to attain this end the histories of 60 patients of the New Haven Hospital, known to have had gall-bladder disease, were surveyed and their gall bladders obtained at operation, were studied The data gathered thus far suggest that there is a relationship between certain types of biliary calculi and the morphological changes in the gall bladder furthermore, that these changes are related to the clinical manifestations

The cases studied were divided, for reasons which will become evident later into three groups (1) patients with "pure gall stones", (2) patients with "mixed gall stones", (3) patients with "combined gall stones "[1]

PATIENTS WITH PURE GALL STONES

Included in this group are patients whose gall bladders contained gall stones consisting entirely or mainly of one of the three stone-forming constituents of the bile (a) cholesterol, (b) pigment calcium (c) calcium carbonate There were 8 of these 7 (6 women, 1 man) whose gall bladders contained solitary pure cholesterol stones and 1 (a 32 year old man) with multiple pigment calcium stones (Table I) The mean age of these patients was 52 5 years All the women had been pregnant one or more times Recent acute attacks of upper abdominal pain lasting from a few days to several weeks were complained of by all the patients with pure cholesterol calculi A history of definite, more or less severe, attacks prior to the acute phase was elicited from only 2 patients, both of whom had had these attacks for several years The patient with pigment calcium stones complained of vague digestive symptoms for 4 to 5 years Normal visualization of the gall bladders by the Graham-Cole method was obtained in one and impaired or no visualization in 5 patients In 2 instances the non-opaque calculi were shown by contrast with the opaque medium filling the viscus

Cholecystitis was observed in the gall bladders of all of the patients with pure gall stones (Table I) The chronic changes were slight and characterized by a small round cell infiltration in the tunica propria and the intermuscular connective tissue the presence of occasional shallow Rokitansky-Aschoff sinuses, some hypertrophy of the muscular coat and a slight increase of the intermuscular and perimuscular connective tissues These changes were noted in all 7 gall bladders which contained cholesterol stones In 3 of these in addition to the slight chronic change, there was a marked acute cholecystitis with edema, polymorphonuclear leucocytic infiltration and extensive hemorrhage and organization In one of the gall bladders (P-1) the mucosa was thrown into plump folds and in the tunica propria of some of the folds large phagocytic cells containing lipoid substances were seen

As mentioned before 7 of the 8 gall bladders of this group contained pure cholesterol stones All of these were solitary, oval, yellow white with a granular surface measuring from 1 7 by 1 3 to 3 2 by 2 2 centimeters Each had a radiating crystalline structure usually about a small center of black brown material The radiopacity of the pure cholesterol calculi was slight In the crevices of some of the crystalline structures, however, there were small amounts of pigment calcium and calcium carbonate which in roentgenograms visualized as radiating lines (Fig 1) The pigment calcium stones present in the one remaining gall bladder were multiple dull black, irregular crystalline structures 1 to 8 millimeters in diameter They fragmented readily into small crystalline masses of calcium salts of bilirubin and bili-

[1] Halpert, Béla New aspects of the formation and classification of gall stones. Arch Path , 19.8 6 6 3

Fig. Solitary cholesterol stone with radiating crystalline structure from the gall bladder of a woman, aged 40 years (P 3)

verdin. They contained no cholesterol and no calcium carbonate. The radiopacity was moderate and homogeneous (Fig. 2). Calcium carbonate stones were not represented in this series.

PATIENTS WITH MIXED GALL STONES

Included in this group are patients whose gall bladders contained gall stones consisting mainly of two or of all three of the stone forming constituents of the bile. The possible varieties of mixed gall stones are: stones consisting of cholesterol and pigment calcium (a + b), of cholesterol and calcium carbonate (a + c), of pigment calcium and calcium carbonate (b + c), and of cholesterol, pigment calcium and calcium carbonate (a + b + c).

There were 44 patients (34 women, 10 men) whose gall bladders contained mixed calculi (*Table II*). *The mean age of these patients* was 46.2 years. Most of the women were obese, the men well nourished. The majority of these patients complained of vague gastrointestinal symptoms for months or years. Some of them had recurrent attacks of acute pain; a few also had jaundice. Thirty of the 44 complained of recent acute abdominal pain. Normal visualization of the gall bladder was obtained in 2, impaired or no visualization in 20 of 22 patients examined by Graham Cole method. Calculi were visualized in only 10

Fig. 2. Pigment calcium stones from the gall bladder of a woman, aged 33 years (P 8)

The morphological changes in the gall bladders of the patients with mixed gall stones were chronic cholecystitis in 29, and chronic cholecystitis with acute exacerbation in the 15 remaining. The chronic changes were characterized by the presence of hernia-like outpouchings of the mucosa, the Rokitansky-Aschoff sinuses, a hypertrophy of the muscular coat, an increase in the connective tissue of the tunica propria and the intermuscular and perimuscular connective tissues and a marked infiltration of all the connective tissue with *small round cells. The hypertrophy of the* muscular coat was manifested by an increase in size and perhaps also in the number of the individual smooth muscle cells and muscle bundles. Usually the muscular coat was thicker over the midportion of the body than over the fundus and neck of the viscus. Where hypertrophy of muscular coat was slight the Rokitansky-Aschoff sinuses were shallow.

The gall bladders of the majority of the patients in this group (38 of the 44) contained calculi composed mainly of cholesterol and *pigment calcium. Admixtures of determin*able amounts of calcium carbonate, calcium phosphate, and iron were also observed in some of these calculi. Usually the central portions contained more of the pigment calcium

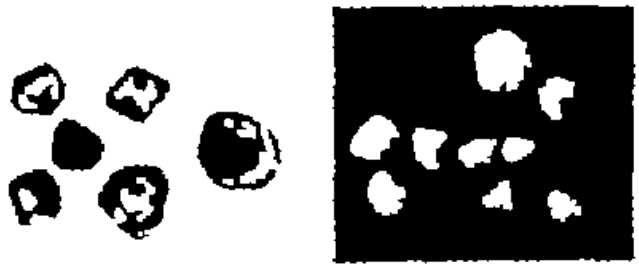

Fig. 3. Cholesterol and pigment calcium (a+b) stones from the gall bladder of a woman, aged 61 years (M 36)

Fig. 4. Cholesterol and pigment calcium (a+b) stones from the gall bladder of a woman, aged 60 years (M 34)

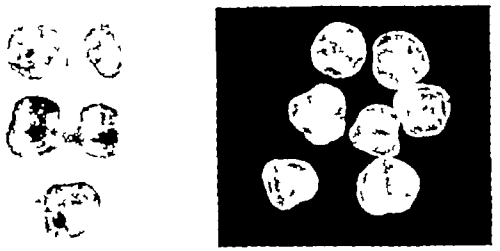

Fig 5 Pigment calcium and calcium carbonate (b+c) stones from the gall bladder of a woman, aged 38 years (M-15)

Fig 6 Pigment calcium and calcium carbonate (b+c) stones from the gall bladder of a woman, aged 61 years (M-38)

than the peripheral (Fig 3) The structure of the latter portion was amorphous or crystalline The smallest stones were numerous and had the appearance of grains of sand Some of these, and more particularly the larger ones, measuring up to 3 centimeters in diameter, were frequently faceted on one two, or more surfaces Their structure was layered or laminated with alternating rings of pigment calcium and cholesterol mixtures in varying proportions Some of the adjacent faceted surfaces of the larger calculi seemed to "articulate" and the opposing surfaces appeared worn In many of the medium sized and large calculi, central fissures were noted (Fig 4) In 5 of the 38 gall bladders, the gall stones, though of similar chemical composition, had a different architecture About single or multiple centers of pigment calcium with little cholesterol, a mass of amorphous cholesterol with little pigment calcium was seen The surfaces of these calculi were roughly granular, light grey or white They were soft and broke easily

The roentgenograms of all the cholesterol pigment calcium stones revealed clearly the absolute and relative distribution of the slightly radio-opaque cholesterol and the moderately radio-opaque pigment calcium

Mixed gall stones composed mainly of cholesterol and calcium carbonate (a+c) were not represented in this series

The gall bladders of 3 patients contained calculi composed almost entirely of pigment calcium and calcium carbonate (b+c) with little if any cholesterol (Figs 5 to 7) They were multiple, round or oval, dark brown or black, very firm, cutting with considerable resistance The surfaces of one set of these stones had a "moth-eaten" appearance (Fig 6) As expected the radio-opacity of the pigment calcium-calcium carbonate stones was more marked than any of the other mixed calculi

The gall bladders of the 3 remaining patients of the group contained calculi composed of relatively great amounts of all three of the stone forming constituents of the bile These cholesterol-pigment calcium-calcium carbonate stones (a+b+c) were also multiple and measured from 4 to 16 millimeters in diameter Their surfaces were smooth or faceted (Fig 8) The distribution of the various stone-forming components varied in the different stones or sets of stones No definite laminations or radiations were noted The radio-opacity was dependent on the relative

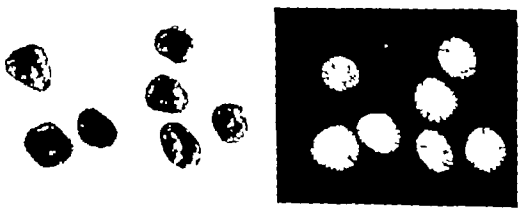

Fig 7 Pigment calcium and calcium carbonate (b+c) stones from the gall bladder of a woman, aged 70 years (M-41)

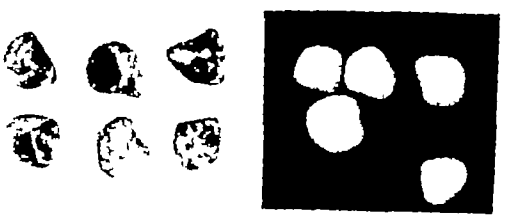

Fig 8 Cholesterol, pigment calcium and calcium carbonate (a+b+c) stones from the gall bladder of a man, aged 53 years (M-29)

TABLE I—PATIENTS WITH PURE GALL STONES

Patient			Prior pancreatitis	Duration of symptoms			Visualization (Graham Cole)	Cholecystitis
No.	Age	Sex		Vague	Recurrent attacks	Recent acute (days)		
Cholesterol (6) stones								
P [illegible]	[illegible]	F		[illegible]		[illegible]	Normal	Chronic, slight
P 2 ([illegible])	43	F	4	[illegible]		[illegible]	Impaired	Chronic, slight, acute, marked with organ [illegible]
P 3 ([illegible])	49	F				[illegible]	Normal	Chronic, slight, acute, marked with organ [illegible]
P [illegible] ([illegible])	[illegible]	F			[illegible]	[illegible]	Normal	Chronic, slight, acute, marked with organ [illegible]
P 5 ([illegible])	64	F		[illegible]	[illegible]	[illegible]		Chronic and acute
P-6 ([illegible])	67	M		[illegible]		[illegible]	Impaired	Chronic, slight
P 7 ([illegible])	75	F				[illegible]		Chronic and acute
Pigment calcium (8) stones								
P 8 ([illegible])	53	M		[illegible]			Impaired	Acute, slight
3 Calcium carbonate (6) stones								

proportion of the more or less opaque components.

PATIENTS WITH COMBINED GALL STONES

Included in this group were patients whose gall bladders contained gall stones which had a nucleus of a pure gall stone and a shell composed of any one or all of the stone forming constituents of the bile. There were 8 patients in this group all women (Table III) The mean age of these patients was 53 2 years Five patients were obese the rest well nourished Two had never been pregnant, the others from 2 to 12 times Most of these patients complained of vague gastro-intestinal symptoms for several years Four had had recurrent attacks of pain but none shortly prior to operation The 4 others complained of recent acute symptoms of a few days or weeks duration Roentgenographic visualization of the gall bladder was impaired in all 4 patients examined Calculi were visualized in 3

The gall bladders of all of the 8 patients with combined gall stones showed chronic changes characterized by the presence of Rokitansky Aschoff sinuses, hypertrophy of the muscular coat an increase of the intermuscular and perimuscular connective tissues and a small round cell infiltration of all the connective tissue In 4 of the 8 gall bladders, there was an acute exacerbation of the inflammatory process

The gall bladders of 4 of the 8 patients in this group contained solitary combined stones which had a nucleus of a pure cholesterol stone with a crystalline radiating structure and a shell composed of layers of varying amounts of cholesterol pigment calcium and calcium carbonate These stones were oval or round measuring from 2 5 by 2 2 to 4 by 3 2 centimeters Their surfaces were finely or roughly granular Roentgenograms of these calculi revealed little structural detail on account of their size and richness in markedly radio-opaque components (Figs 9 and 10)

The gall bladders of the 4 remaining patients contained in addition to one large combined stone one or more smaller mixed stones The chemical composition and the architecture of the latter was the same as that of the shell of the large combined stone This was evident on the cut surfaces as well as on roentgenograms (Figs 11 and 12)

DEDUCTIONS

Gall stones of similar chemical composition and architecture are perhaps produced by disorders of the same kind and are likely to pre-

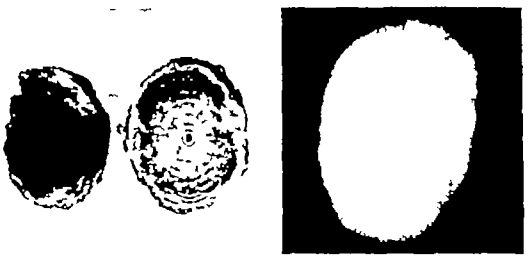

Fig 9 Combined gall stone from the gall bladder of a woman, aged 61 years (C-6) About a cholesterol nucleus alternating layers of pigment calcium and cholesterol are desposited

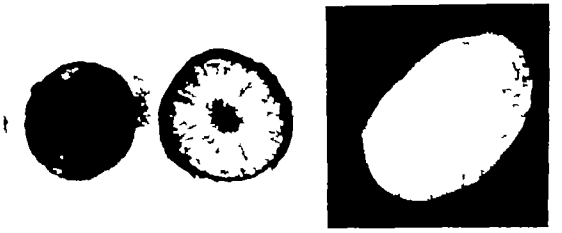

Fig 10 Combined gall stone from the gall bladder of a woman, aged 72 years (C-8) A cholesterol stone with radiating crystalline structure forms the nucleus and layers of pigment calcium and cholesterol the shell

sent the same set of clinical manifestations This line of thought suggested that for the purpose of analysis, those patients whose biliary disorders resulted in the formation of gall stones of identical type, should be grouped together

The 60 cases in this study were not selected and therefore comprise a random sample of patients with gall-bladder disease There were 8 patients with pure, 44 with mixed, and 8 with combined gall stones

In the patients with pure gall stones the clinical manifestations of gall-bladder disease were rather recent and the morphological changes in the gall bladder were either acute, or acute superimposed upon a slight or moderate degree of chronic change These facts suggest that in this group of patients the cholecystitis followed rather than preceded the stone formation

Most of the patients with mixed gall stones had recurrent attacks of acute abdominal pain The prevalent morphological change in the gall bladders of this group was chronic cholecystitis This was usually characterized by the presence of Rokitansky-Aschoff sinuses, hypertrophy of the muscular coat, and an increase in the connective tissue of the tunica propria and the intermuscular and perimuscular connective tissues, all of which showed a small round cell infiltration Superimposed upon these chronic changes, there was in many instances an acute inflammatory process The composition, structure, and size of the calculi in each gall bladder showed marks of the successive changes of their evolution All of this suggests a causal relation between the chronic cholecystitis with recurring acute exacerbations and the formation of mixed gall stones

In patients with combined gall stones the clinical manifestations as well as the morphological changes in the gall bladder were quite similar to those observed in patients with mixed gall stones Combined gall stones although older and usually larger rarely caused more severe clinical manifestations than mixed gall stones of smaller size The nucleus of a combined stone is, of course, older than its shell and therefore it seems reasonable to assume that the process which led to the for-

Fig 11 One combined and several mixed calculi from the gall bladder of a woman, aged 71 years (C 7) The nucleus of the large stone is of pigment calcium and calcium carbonate (b+c) with a shell of cholesterol and pigment calcium

Fig 12 One combined and several mixed calculi from the gall bladder of a woman, aged 45 years (C-3) The nucleus of the combined stone is of cholesterol, the shell is of pigment calcium and calcium carbonate rich in cholesterol (a+b+c) The structure and composition of the mixed calculi are identical with those of the shell of the combined stone

TABLE II—PATIENTS WITH MIXED GALL STONES

Patient			Pregnancies	Duration of symptoms			Cholecystograms (Graham-Cole)	Conclusions
No.	Age	Sex		Vague	Recurrent attacks	Typical acute attack		
Cholesterol and pigment calculi (+++) stones								
[illegible]	[illegible]	F			[illegible] mos	wk		Chronic with slight acute exacerbation
[illegible]		F	[illegible]		[illegible] mos		Poor	Chronic
[illegible]	[illegible]	F	[illegible]			wk		Chronic with acute exacerbation
[illegible]	[illegible]	F	[illegible]	[illegible] mos	[illegible] mos		Impaired	Chronic
[illegible]	[illegible]	F				wks.		Chronic
[illegible]	[illegible]	F	[illegible]		yr	wks		Chronic
[illegible]	[illegible]	F	[illegible]		[illegible] yrs.	days		Chronic
[illegible]	[illegible]	F	[illegible]	[illegible] yrs	[illegible] yrs	days		Chronic with acute exacerbation
[illegible]	[illegible]	F		yrs	yrs	days	Normal	Chronic, slight
[illegible]	[illegible]	F	[illegible]		[illegible] mos		Poor	Chronic, slight
[illegible]	[illegible]	F	[illegible]	years				Chronic
[illegible]	[illegible]	F			yrs.	weeks	Impaired	Chronic
[illegible]	[illegible]	F	[illegible]	years	[illegible] mos	days	Poor	Chronic, marked
[illegible]	[illegible]	M		years		days		Chronic
[illegible]	[illegible]	F	[illegible]	yr		days		Chronic with acute exacerbation
[illegible]	[illegible]	F	[illegible]		[illegible] yrs		Impaired	Chronic
[illegible]		F		years	yrs	day	Poor	Chronic with acute exacerbation
[illegible]	[illegible]	F		mos	yrs		Impaired	Chronic
[illegible]	[illegible]	M		years		mos		Chronic, slight
[illegible]	[illegible]	F	[illegible]		years			Chronic, marked
[illegible]	[illegible]	F	[illegible]	years	yr	days	Poor	Chronic with acute exacerbation
[illegible]	[illegible]	F		mos	mos		Impaired	Chronic, marked
[illegible]	[illegible]	F	[illegible]	[illegible] yrs.	years			Chronic, marked
[illegible]	[illegible]	F		[illegible] yrs	years	weeks		Chronic, marked with slight acute exacerbation
[illegible]		F	[illegible]	[illegible] yrs		mos	Normal	Chronic, slight
[illegible]	[illegible]	M		yrs	yrs	days		Chronic with acute exacerbation
[illegible]	[illegible]	M		[illegible] yrs		[illegible] days		Chronic with acute exacerbation
[illegible]	[illegible]	F		mos		days	Poor	Chronic with slight acute exacerbation
[illegible]	[illegible]	F		yrs	[illegible] yrs.	[illegible] wks	Impaired	Chronic
[illegible]	[illegible]	M		yrs	yrs	weeks		Chronic
[illegible]	[illegible]	F		[illegible] yrs	[illegible] yr	days	Poor	Chronic with acute exacerbation subsiding
[illegible]	[illegible]	F		weeks		days		Chronic
[illegible]	[illegible]	M		[illegible] yrs	years		Poor	Chronic
[illegible]	[illegible]	F	[illegible]	years	years		Impaired	Chronic, marked
[illegible]	[illegible]	M		years		day		Chronic with acute exacerbation
[illegible]	[illegible]	F	[illegible]	[illegible] yrs	[illegible] yrs.		Impaired	Chronic marked
[illegible]	[illegible]	F	[illegible]	years	years	days	Impaired	Chronic
[illegible]	[illegible]	M		years	yrs	days		Chronic with acute exacerbation
Cholesterol and calcium carbonate (+++) stones								

TABLE II.—PATIENTS WITH MIXED GALL STONES—Continued

Patient			Pregnancies	Duration of symptoms			Visualization (Graham Cole)	Cholecystitis
No	Age	Sex		Vague	Recurrent attacks	Recent acute attack		
3 Pigment calcium and calcium carbonate (b+c) stones								
M 15 (10,425)	38	F	5			1 mo	Impaired	Chronic
M-38 (11,395)	61	F	2	years	15 yrs.		None	Chronic, slight
M 41 (10 905)	70	F	2		1 yr			Chronic
4 Cholesterol pigment calcium and calcium carbonate (a+b+c) stones								
M 26 (10,693)	50	F	2	years	10 yrs	weeks		Chronic
M 29 (10,731)	53	M		mo		days	Impaired	Chronic with acute exacerbation
M 44 (0,461)	73	M			1½ yrs.	days		Chronic with acute exacerbation

TABLE III.—PATIENTS WITH COMBINED GALL STONES

Patient			Pregnancies	Duration of symptoms			Visualization (Graham-Cole)	Cholecystitis
No	Age	Sex		Vague	Recurrent attacks	Recent acute attack		
C-1 (10 249)	40	F	0	2 yrs	3 yrs.		Impaired	Chronic
C-2 (10,259)	44	F	2	4 yrs.	4 yrs	weeks	Impaired	Chronic with acute exacerbation
C 3 (10,794)	45	F	4	6 mos	6 mos.			Chronic
C-4 (10,841)	47	F	8	5 yrs		2 days		Chronic with acute exacerbation
C-5 (10,146)	56	F	0		3 mos			Chronic with acute exacerbation
C-6 (9,373)	61	F	5	years		weeks	Impaired	Chronic
C-7 (9 114)	61	F	2		5 yrs			Chronic
C-8 (9,106)	72	F	12	years		2 days	Impaired	Chronic with acute exacerbation

mation of the nucleus preceded that which formed the shell

SUMMARY

An attempt was made to correlate the clinical manifestation of cholecystitis and cholelithiasis with the morphological changes in the gall bladder and its content Those patients whose biliary disorders resulted in the formation of gall stones of similar type were grouped together

In the patients with pure gall stones, the clinical manifestations of gall-bladder disease were rather recent and the morphological changes in the gall bladder were either acute, or acute superimposed upon a slight or moderate degree of chronic change It was, therefore, assumed that in this group of patients the cholecystitis followed rather than preceded the stone formation

In the patients with mixed gall stones, the clinical manifestations of gall-bladder disease were of a chronic nature with recurrent acute attacks The gall bladders of this group showed evidences of chronic cholecystitis and in many instances a superimposed acute inflammatory process It was, therefore, assumed that a causal relation existed between the chronic cholecystitis with recurring acute exacerbations and the formation of mixed gall stones

In the patients with combined gall stones, the clinical manifestations as well as the morphological changes in the gall bladders were quite similar to those observed in patients with mixed gall stones

LIFE EXPECTANCY IN BILIARY INTESTINAL ANASTOMOSIS

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ONE of the occasions upon which the surgeon is called to exercise his most astute judgment is when presented with an obstruction of the common duct that can not be removed with reasonable safety to the patient. If the gall bladder is present and the cystic duct is open, a cholecystogastrostomy or cholecystoduodenostomy offers an escape from a difficult situation. In other instances, the common duct or even the hepatic duct must be used for the anastomosis. The surgical textbooks and operative manuals merely mention these operations, or describe the technique giving nothing as to the results. The recent surgical systems (35, 72) warn against the danger of ascending liver infection and imply that the life expectancy is short.

The first cholecystenterostomy was reported by Winiwarter in 1882. In 1894, Michaux reported a cholecystoduodenostomy done by Ricard. The patient died 53 days later with cholangitis. In the same year Dujardin and Beaumetz reported a case of Charcot's intermittent hepatic fever following cholecystoduodenostomy. Since these original observations, there have been many reports of different types of operations for anastomosis of the biliary and gastro-intestinal tract and many opinions expressed as to the presence or absence of cholangitis as a serious complication.

EXPERIMENTAL RESULTS

From the experimental standpoint cholangitis with ascending liver infection seems to be an almost constant finding following biliary-intestinal anastomosis in dogs (24, 30, 40). Marinelli, however reports that cholecystogastrostomy produces less liver infection than cholecystoduodenostomy. It has been pointed out that the gall bladder of the dog has accessory ducts which would increase the tendency to ascending liver infection. It is interesting to note that one monkey sacrificed 8 months after cholecystogastrostomy presented no liver infection (70). On the other hand Gage working in New Orleans, reported liver infection in 100 per cent of normal dogs, and that only 46 per cent of his dogs sacrificed 15 days after cholecystoduodenostomy had more liver infection than normal. Recently Gentile published the results of experiments in dogs from which he concluded that ascending liver infection is not a danger after cholecystogastrostomy. Reasoning that the nature of a dog's food and habits made previous experiments not applicable to man, he divided the stomach, making a blind pouch of the distal end and connecting the proximal end to the jejunum. At a second operation the gall bladder was anastomosed to the gastric pouch which was now separate from the current of food. He felt that such an arrangement more nearly approached bacteriologically what one finds in the human. The dogs were sacrificed 40 to 97 days after the second operation. He found no greater liver infection than before the cholecystogastrostomy was performed. These experiments are subject to the objection that there is no opportunity for reflux of food into the gall bladder such as does occur in the human (7, 8, 65).

TYPES OF OPERATIONS

It is generally agreed that the position of the anastomosis should by choice be in the stomach or duodenum rather than lower in the gastro-intestinal tract because there is less danger of ascending biliary infection. There seems to be little choice between the stomach and duodenum. The latter is preferred by many because it more nearly simulates the normal. Experience has definitely shown, however that cholecystogastrostomy is well tolerated (31). Many prefer it as they feel that it is a safer operation and liver infection is less likely than with cholecystoduodenostomy. Alexandroff from cases collected from the literature between 1880 and 1918, compiled the figures shown in Table I.

TABLE I

Anastomosis of gall bladder to—	Cases	Mortality
Stomach	102	13
Duodenum	102	18
Small Intestine	257	34
Large Intestine	29	49

Most surgeons prefer to use the gall bladder for the anastomosis when it is accessible Finsterer, however, removes the gall bladder to prevent further stone formation and does a choledochoduodenostomy In support of such an operation is the fact that stones have formed in the gall bladder after cholecystoduodenostomy and caused obstruction of the anastomosis with resultant jaundice (53) In cases of deep jaundice, Walters (67) suggests performing the operation in two stages We have found this of value

Many methods of anastomosis have been suggested Some do a simple lateral anastomosis (65), others use a button (52) or a rubber (16, 51) or metal (59, 61) tube Roeder (60) suggested performing a plastic operation on the gall bladder to form a tube which is carried through the walls of the stomach to produce a valve-like action However, he reported 2 patients who died with liver abscesses after this type of operation Mason (44) also suggested an operation with this in view, but later, with Baker (45) reported a death with multiple liver abscesses after his operation We have used a permanent tube in the gall bladder as described by Muller However, cases have been reported in which the tube has become obstructed by deposits of bile salts (33) Finsterer emphasizes the importance of a wide opening and at the same time denies that the operation increases the danger of ascending infection It seems likely that cholangitis would be best tolerated in the presence of a wide opening with adequate drainage

A few successful indirect anastomoses have been performed, but these operations are still more or less curiosities Such operations are, of course, done only as a last resort and carry a high percentage of failure Jenckel reported the first indirect hepaticoduodenotomy when his patient was still well 4 years after operation Odermatt recorded a case with death from cholangitis 6 years after a similar operation Williams and Smithwick reported a patient well 16 years after the transplantation of a fistulous tract into the duodenum Lahey has 2 cases of a similar nature well 7 and 8 years after operation A complete monograph of the various types of operations on the biliary ducts has been published by Horgan

INDICATIONS FOR OPERATION

The average surgeon has done a biliary intestinal anastomosis only when he has been forced into it The indication is usually a common duct obstruction from carcinoma of the pancreas or bile ducts, chronic pancreatitis stricture or traumatic injury of the ducts or a stone in the common duct that cannot be removed Since Babcock's publications in 1920, a number of surgeons, especially in Europe, have performed cholecystogastrostomy for peptic ulcer To this list of indications, Du Bose has added perforated gall bladder, acute pancreatitis, chronic obscure jaundice, perforated peptic ulcer, and marginal ulcer following gastrojejunostomy Bérard and Mallet-Guy have performed cholecystogastrostomy in certain cases which they term pseudolithiasis due to cholecystic intolerance feeling that such an operation gives better results than cholecystectomy Steel recommends cholecystogastrostomy as a routine procedure in gall-bladder disease in preference to cholecystectomy Blos has used the operation as a method of obtaining proper drainage in cases of cholangitis with liver infection Heyd has obtained encouraging results with cholecystoduodenostomy in acute liver degeneration He reasoned that the operation gave a lymphatic pathway of escape for lymph and edema from the liver

The object of cholecystogastrostomy in gastric ulcer is, of course, to establish a steady flow of alkaline bile over the ulcer site Sippy has pointed out, however, that about seven to nine times the normal output of bile would be required to neutralize the gastric juice, since the daily output of bile is about 1000 cubic centimeters the hydrogen ion concentration being 7 4, while the stomach secretes about 1500 cubic centimeters of fluid with a hydrogen ion concentration of 1 2–2 0 Archibald, as a result of animal experimentation, contends that cholecystogastrostomy does not

TABLE II

Cases		Results	
Cholecystoduodenostomy	44	Operative deaths	[illegible]
Malignancy	18	Lived [illegible] months	
Chronic [illegible]	20	Lived [illegible] years	1
		Died cholangitis in [illegible] years	
Chronic pancreatitis, no stone	11	Lived [illegible] years)	
		Died of cholangitis	
Stricture	4		
Cholecystogastrostomy	11	Operative deaths	3
Malignancy	10	(Life [illegible] months)	
		Died of cholangitis	
Chronic pancreatitis, no stone	1	Lived [illegible] years	
Cholecystojejunostomy	38	Operative deaths	5
Malignancy	7	Complete failures	5
		Died of cholangitis 8–17 years	1
Stenosis of common duct	20	Died of other causes	1
		Average 13 years	
		Occasional severe cholangitis	
Chronic pancreatitis	19	Well [illegible] years	[illegible]
		Occasional mild cholangitis	9
Miscellaneous			
Repeated [illegible] in 4 previous operations		Operative deaths	3
		Well [illegible] years	1
		Occasional mild cholangitis	1

divert the flow of bile through the stomach as long as the common duct is not obstructed The Mayos (48) called attention to this in 1908. Beaver reported that cholecystogastrostomy had no effect upon the gastric acidity in the dog Kagan, however gives the data on 3 patients in whom the gastric acidity was lowered after such an operation Judd and Parker (36) and Babcock (4) agree with this conception It is perhaps of some interest that Walzel reported a jejunal ulcer following the performance of a cholecystogastrostomy and gastrojejunostomy at one operation

CLINICAL RESULTS

Although theoretical considerations and laboratory experiments may help a great deal the final decision as to the value of an operation must come from the actual effect upon the patient This however is not always easy to determine since failures are not so frequently reported as successes

In the case of cholecystogastrostomy for peptic ulcer Babcock (3) Braithwaite Nazarov and Frenkel report satisfactory results Frenkel (22) published the only series in which there were follow up reports He reported 68 operations with 1 death. Thirteen were not followed The 54 remaining were followed for from 6 months to 5 years. The results in 35 were classed as excellent, in 11 as fair and in 8 as poor None of these writers has reported ascending cholangitis as a complication of cholecystogastrostomy for peptic ulcer This, of course, again brings up the question as to whether the anastomosis persists when the common duct is open. Nazarov reoperated upon 3 of his patients when symptoms returned and he found the anastomosis closed. Since his other cases had no return of symptoms, he assumed that the anastomosis was functioning Steel had occasion to reoperate upon 4 cases in which cholecystogastrostomy had previously been done for gall-bladder disease without jaundice The anastomosis was still open in all 4 cases

The major rôle for biliary intestinal anastomosis comes in cases of common duct obstruction. When the obstruction is due to malignancy the surgeon performs the anastomosis as a palliative measure. However when the obstruction is of a non-malignant nature, the surgeon is unwilling to subject his patient to any unnecessary danger such as ascending biliary infection It is, therefore, of the utmost importance that the success of biliary intestinal anastomosis as to life expectancy be evaluated If it is true as some contend that cholangitis is never a complication the surgeon can save much time and trouble in the region of the common duct by simply doing a cholecystoduodenostomy or cholecystogastrostomy On the other hand if "serious infection of the liver is an almost inevitable consequence as stated by Graham Cole Copher and Moore the operation must be done only as a last resort

That the operation is not a cure-all is apparent from the fact that spontaneous biliary intestinal fistulas usually require surgical intervention As a result of their experience at the Mayo clinic with 153 spontaneous biliary fistulas (117 duodenal) which required operative relief Judd and Burden (34) concluded that the "formation of a spontaneous internal biliary fistula is in no sense a cure of cholelithiasis, but is an additional and dangerous complication."

In this country Babcock (3) and Du Bose (18) both of whom have had a large experience with the operation state that they have never seen cholangitis following cholecystenterostomy In Europe, Finsterer Loewenstein and Bardeleben agree that it is not a

is a frequent complication but that its frequency is not great enough to cause the operation to be discarded. Such men are Mayo Robson Kehr and Bernhard. Many other writers (26 69 35, 45 60 72) have considered ascending infection as a major drawback to the operation, and have given case reports in which multiple small periductal abscesses were found in the liver at autopsy

Bernhard made a report of 128 cases which have a more complete follow up than those of any other report in the literature. It is given in detail in Table II.

Table III gives briefly the experience of some of the writers as reported by them. It also includes the interval since operation in the longest followed case. The feeling of the writers in regard to cholangitis as it affects life expectancy is noted.

In Table III 10 cases previously unreported are given under the name of the senior author Malignancy was the cause of the common duct obstruction in half of the cases. The results are as follows

	Cases
Died in the hospital	4
Died of cholangitis 1 year after operation	1
Not traced	
Well 6 and 3 months after operation (latter malignant)	
Well 8 years after operation	1

One of the patients who died from cholangitis had a carcinoma of the bile ducts at the junction of the cystic and hepatic ducts A hepaticoduodenostomy was done At autopsy 1 year later there was no recurrence of the carcinoma and there were multiple periductal abscesses of the liver The tube used for the anastomosis was still in place. Autopsy was not performed on the second cholangitis case but the clinical picture was typical The patient well at 6 months was a case of stone in the common duct The stone could not be removed by choledochostomy so at a second operation a cholecystoduodenostomy was done. The fistula from the common duct was also transplanted into the duodenum The patient well 8 years after operation had a traumatic stricture of the common duct. A cholecystoduodenostomy was done About 1 years after operation, the patient was severely jaundiced for 3 months but recovered spontaneously She has had no jaundice since then. A recent X-ray film showed that the tube used for the anastomosis was no longer present.

CONCLUSIONS

1 The operation cholecystogastrostomy or cholecystoduodenostomy has a definite place in surgery in cases of common duct obstruction.

2 Its usefulness in other conditions can not be properly evaluated at the present time.

3 In cases of malignant obstruction of the common duct the life expectancy may be increased only a few months on the average Life is made more bearable, however by the relief of the jaundice

4. In cases of non-malignant obstruction of the common duct, the life expectancy has been normal in many instances A number of patients have died within a few years, of ascending liver infection The average life expectancy cannot be accurately evaluated.

5 Ascending liver infection is a frequent enough complication of the operation to prevent its indiscriminate use.

6 In a poor surgical risk, cholecystogastrostomy or cholecystoduodenostomy is preferable to a long surgical procedure, especially when the removal of the common duct obstruction may be difficult or impossible.

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PANCREATIC FISTULA

A Case With Intubation of Wirsung's Duct

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THE study of pure external pancreatic secretion in the human being has been confined to the cases with pancreatic fistulas such as follow the drainage of pancreatic cysts, traumatic rupture of the pancreas accidental injury to this gland during upper abdominal operations, and the intubation of Wirsung's duct Of the latter we have been able to find only one case in the literature, that of Glaessner (8), who in a resection for carcinoma of the duodenum in 1904 cut across the pancreatic duct and put a tube in it leading to the outside of the abdomen Because of the rarity of this condition, we wish to report a similar case in which Wirsung's duct was intubated after a resection of a carcinoma of the common duct

The patient, Mr F K, a truck driver of 48, was admitted to the Medical Service on March 31, 1934, complaining of jaundice of 12 weeks' duration He had been well until 13 weeks before entry when he became somewhat nauseated and vomited 3 to 4 hours after every meal His local physician took several X-ray films which were negative for gall stones or visible mass He had lost about 35 pounds in weight since the onset of his present illness

Physical examination revealed a fairly well developed man deeply jaundiced The liver edge was felt three fingers below the costal margin His urine was positive for bile, but the stools were green on several examinations Wassermann was negative, non-protein nitrogen, 32 milligrams per cent, blood cholesterol, 209 milligrams per cent, Van den Bergh direct reaction 22 50 milligrams per cent, bleeding time 2 5 minutes, clotting time, 9 minutes, sedimentation rate, 38 millimeters in 30 minutes, red blood count, 3,190,000, hemoglobin, 60 per cent (Sahli) X-ray examination of the stomach and duodenum could not establish a diagnosis of carcinoma of the head of the pancreas and a surgical consultation advised exploration

The patient was explored under local anesthesia, and a firm tumor was palpated at the ampulla of Vater which seemed to be about 1 5 centimeters in diameter and to occlude the common duct Cholecystoduodenostomy with drainage of the common duct was done (Fig 1)

The patient made an excellent recovery, his jaundice nearly disappeared, and he gained 10 pounds in weight Five weeks after the first operation he was operated upon again and a transduodenal excision of a tumor at the ampulla of Vater was done Pathological studies showed it to be a carcinoma probably originating in the common duct As the tumor was drawn down through the posterior duodenal wall its upper attachments were found to consist of common duct and the upper portion of this pedicle was tied off In the lower part of the pedicle a large pancreatic duct had been cut across, which was taken to be the duct of Wirsung, and into it a No 10 French catheter was inserted and sutured. The incision in the posterior wall of the duodenum was then closed about the tube which was led across the duodenum and through the transverse incision in its anterior wall and out through a stab wound in the abdominal wall The final arrangement with the tube in place is shown in Figure 1

With the exception of some pain in the left flank for one day following operation and a mild febrile reaction on the eleventh day, the patient made an excellent recovery and ran a perfectly smooth course He was discharged home on the twenty-second day after operation He has since had a local recurrence which necessitated further operative procedure, but he recovered from this satisfactorily and left the hospital in fair condition

REPORT OF STUDIES IN PANCREATIC JUICE

During the 11 days following the second operation we obtained pure pancreatic juice from the catheter placed in the duct of Wirsung Our investigations dealt with (1) quantitative studies, on the output of pancreatic secretion, (2) the effect of drugs on the flow of secretion from the pancreas, and (3) qualitative studies on the enzymatic content and chemical constituency of the pancreatic juice

1 *Quantitative studies A Average daily output* During the last 4 days of our experiment the patient had an average daily output of 1,167 cubic centimeters, although during this time there was a definite rise from day to day until on the last day we obtained 1,384 cubic centimeters This represents the response to a fairly adequate diet in a convalescing man of 150 pounds Chart 1 shows the daily output of pancreatic juice from

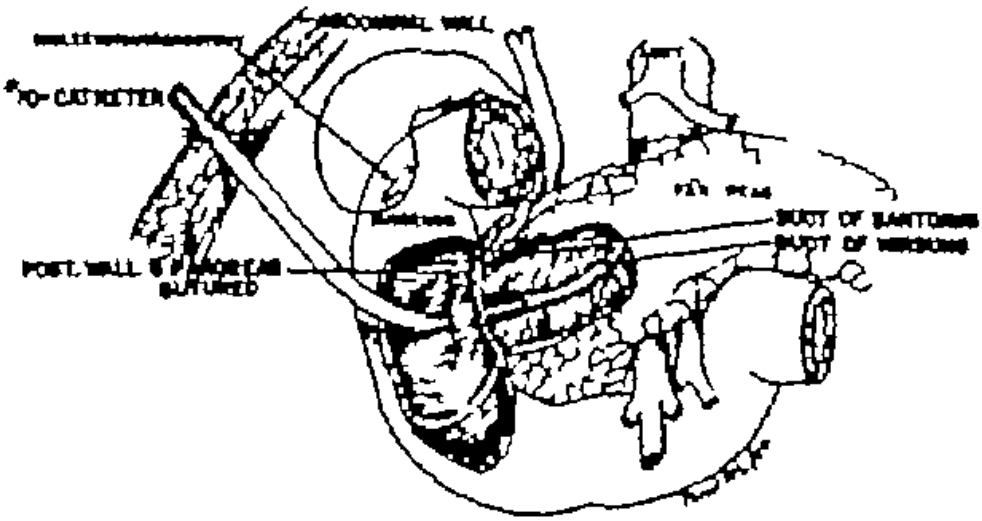

Fig Anatomical relationships after operation.

8 p m. to 8 p.m. We are unable to explain the marked decline on the sixth and seventh days, but we know that during this period the response of the organ was grossly irregular when compared with the results obtained on other days.

B Effect of digestion. Regardless of the activity of the gland, the minute to minute output of the pancreas varies considerably The number of drops per minute recorded every 3 minutes for an hour while the gland was actively secreting varied from 12 to 20 A perfectly obvious though significant fact is that the main portion of the pancreatic secretion comes during the day when the patient is digesting food. The average output during the day was double that at night. Minute readings were made to determine the time required for the pancreas to respond to a food stimulus When 65 cubic centimeters of milk were given the response went in 3 minutes from 5 to 19 drops per minute. The hourly volume for this same feeding is shown in Chart 2 Chart 3 gives graphs for a similar experiment with concentrated glucose and demonstrates a delayed response which might be explained by a slower emptying of the stomach owing to the reflex closure of the pylorus caused by concentrated glucose (Shay Gershon-Cohen 28)

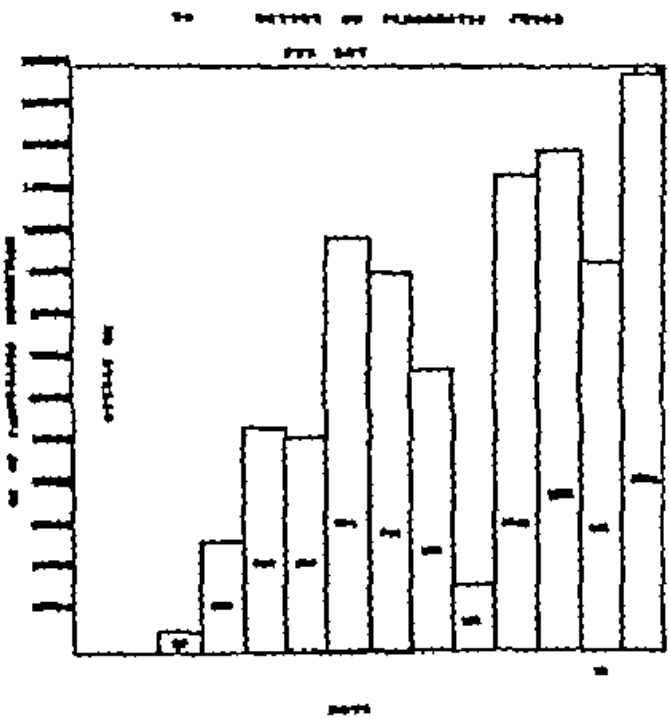

Chart 1 Twenty four hourly output of pancreatic juice

C Continuous secretion During the last 4 days of our experiment there was only a very rare hour in which there was not at least a few cubic centimeters of pancreatic secretion.

D Effect of different foodstuffs It is difficult to draw conclusions from our experiments as to the effects of the 3 main types of foodstuffs upon pancreatic secretion. In analyzing our figures we found only one instance of what could actually be considered a pure meal with adequate control However we did feed our patient meals composed predominantly of fat carbohydrates, and proteins and noted the results of pancreatic secretion.

On a fasting stomach we gave 50 grams of glucose in 3 ounces of syrup The secretion curve is shown in Chart 3 and corresponds

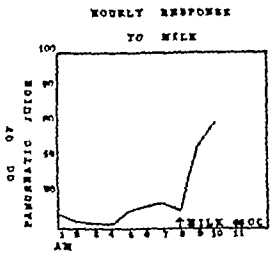

Chart 2 Effect of milk on the response of the pancreas

closely with those of Holsti and Wohlgemuth except for a slightly delayed response which can be explained on the delayed emptying time of the stomach caused by hypertonic solutions (Shay, Gershon-Cohen, 28)

E Effect of water In many instances water given independently of food causes almost immediate stimulation of pancreatic secretion (see Chart 3) This can be explained on the findings of Ivy that if water is placed in the stomach and immediately withdrawn, 5 to 10 cubic centimeters are always lost and have passed along with secretagogues into the duodenum

2 *The effect of drugs A Ether narcosis* For 5 hours after ether administration, there was no secretion from the pancreas This is in accord with experiments on dogs which indicate a depressant effect on pancreatic secretion by ether narcosis (Zucher et al)

B Atropine The results on three experiments with 1/100 grain of atropine given subcutaneously showed the effect illustrated in Chart 4 In addition to a generally diminished output, the expected hourly rise after meals was converted into a diminution by atropine, the duration of its effect being about one hour

C Pilocarpine Pilocarpine seems to increase the output of pancreatic juice On two occasions 1/100 grain was given subcutaneously and marked increase in the number of drops per minute noted The duration of its effect was also about 1 hour

D Physostygmine Physostygmine was found to have the same effect as pilocarpine on the one occasion that it was administered in the dose of 1/100 grain

E Secretin We prepared some secretin from the intestinal mucosa of freshly killed

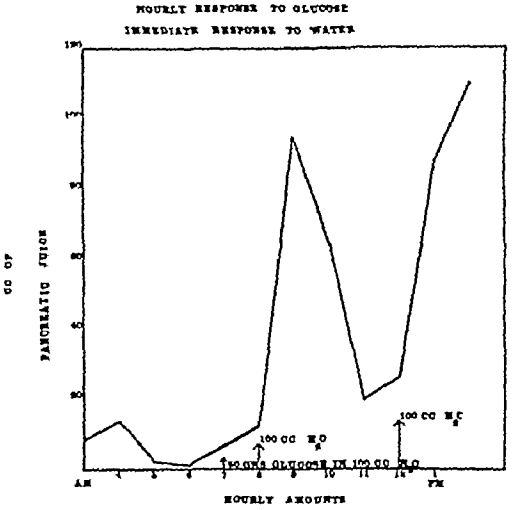

Chart 3 Effect of glucose on the pancreatic secretion

hogs according to the method of Weaver, Luckhardt, and Koch After testing it on ourselves for toxic properties we injected 6 milligrams of the purified extract intravenously, but without conclusive results We prepared a second batch of secretin and intended to give a much larger dose, but the patient refused to have it injected

3 *Qualitative studies A Gross appearance* In the main the secretion which we obtained from the pancreatic fistula was a clear, watery fluid Sometimes it had a slightly ground-glass appearance and contained tiny solid particles Occasionally it had a slightly yellowish tinge That this might be due to bile

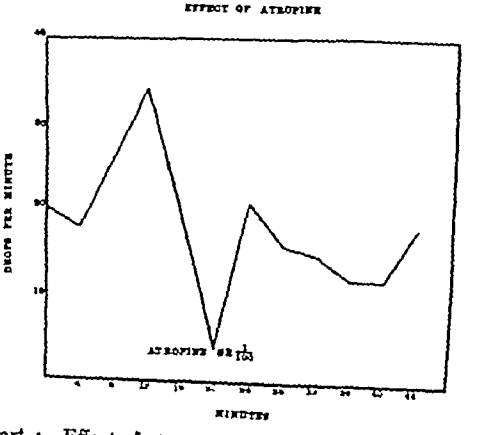

Chart 4. Effect of atropine on the pancreatic secretion.

TABLE I — AMOUNTS OF PANCREATIC JUICE IN 24 HOURS

Investigator	Volume of secretion in cubic cm	
Ellinger and Cohn	[illegible]	
Glassner	[illegible]	
Glassner and Popper	[illegible]	
Graf	[illegible]	
Hedenius	[illegible]	
Kahn	[illegible]	
Kahn and Klein	3 days over [illegible]	Average for 3 days [illegible]
Kaminski	[illegible]	
Kroiss	[illegible]	Almost [illegible]
Mossmann	170–600 (average [illegible]) for three [illegible]	
Mossmann	[illegible]	
Mosse	[illegible]	
Pick	[illegible]	
Schlesinger	[illegible]	
Villard and Jaboy	[illegible]	
Villard and Jaboy Remainder	[illegible]	
Von Friedrich	[illegible]	
Oser	[illegible]	

would be possible only by regurgitation from the duodenum (Fig 1) but we do not believe this to be the explanation since we gave methylene blue by mouth but found no coloring in the secretion secured and furthermore tests on the few yellow specimens obtained with nitric acid and Lugol's solution were negative for bile.

B Specific gravity The average specific gravity for all specimens was 1.012 The highest specific gravity 1.019 was obtained after a 7 hour period of fasting although a high reading was not a constant finding in the fasting secretions. There was no appreciable difference in the specific gravity of the juice obtained after predominantly carbohydrate fat or protein meals or after subcutaneous injection of pilocarpine.

C Reaction and hydrogen-ion concentration The pancreatic secretion was definitely alkaline. The average hydrogen-ion concentration was 8.6 (10 specimens)

D Enzymatic action There were present active lipolytic, amylolytic, and proteolytic enzymes in all the specimens of pancreatic juice examined We adapted the chemical analysis outlined by McClure Whitmore and Reynolds, for estimating the enzymatic activities of duodenal contents and cannot therefore compare our results with those of some of the other investigators in this field (Table III) The lipolytic activity was measured by titrating the amount of butyric acid formed on the addition of the pancreatic secretion to cotton seed oil. Amylolytic activity was based on the production of erythrodextrins in starch solutions and color estimations on the introduction of iodine Proteolytic activity was based on the determination of the amount of non-protein nitrogen present in a measured amount of casein after the addition of pancreatic juice A rough estimation of the proteolytic enzymes present was also made by measuring its action on Mietz tubes. In 5 millimeter glass tubes there is an average of about 2 millimeters of casein broken down in 24 hours with fresh pancreatic juice. No significant difference occurred with the secretions following special meals Addition of enterokinase did not increase the activity The enzymatic activity diminishes on standing in all the samples we examined

REVIEW OF THE LITERATURE

1 Volume of pancreatic juice Ellinger and Cohn were the first to notice that the secretion of pancreatic juice in humans is continuous, a finding which has been confirmed by a number of other investigators (1 9, 12 14 30) One observer noted no great difference in secretion between the active and restive states of the patient (12) while another found that on the same dietary regimen 107 cubic centimeters were secreted in the resting condition as compared with 185 cubic centimeters during the active state. Fever diminishes pancreatic secretion (7 12) As early as 1875 Lacompte showed that pancreatic secretion is least during fasting and most after a meal and that the increased activity lasts 4 hours after taking food This finding has been repeated in practically all the cases studied.

We have no accurate figures on the volume of total pancreatic secretion in 24 hours for the human being. Table I shows the 24 hour amount obtained in some of the cases with fistulas which we have reviewed but it must be remembered that these investigations represent only partial secretion

The highest figure is that obtained by Kahn and Klein although this is closely approximated by Kroiss and by Mossmann. Glassner had a tube in the duct of Wirsung but this may not mean that total secretion was obtained in that the duct of Santorini often drains a good part of the pancreatic juice into

TABLE II—CHEMISTRY OF PANCREATIC JUICE

Author	H-O%	Total Solids	Sp gr	N	Coag Prot	Alc. sol Prot	Glob	Alb	pH	Ash	Fr P
Ellinger and Cohn	98 8618 98 7386	1 1182 1 2614	1 008 1 008	0 084 0 0065	0 1374	0 4240	0 0496	0 0218			
Friedrich	98 749	1 251	1 010 1 013	0 075			0 075	0 152	8 10 F 8 45–8 5	0 5974	0 52
Glaessner	98 7 92 98 7816	1 2706 1 2494	1 0074 1 0075	0 0981 0 0842	0 1744 0 1,6	0 5050 0 4216	0 0655 0 0410	0 1070 0 0566	after food		
Glaessner and Popper			average 1 009	Kjeldahl 0 504							0 51
Holsti		1 4	1 010 1 015	0 08						0 58	
Kahn and Klein		2–1% 1% org	1 005						8 2		
Riesne.		1 86	1 009								
Schumm	98 4551	1 5449	1 009	0 0804	0 090	0 5611				0 8547	
Vilard and Labry		1 300	1 014							950	

the duodenum as noted by various investigations (4, 26, 23) The amount obtained from any fistula will necessarily vary with the anatomical location—the largest amounts being obtained when the fistula drains a large duct

The detailed analysis of the volume output of pancreatic juice has been devoted to a determination of the total amount and secretion curves that result when pure food stuffs are fed In animals Pawlow found carbohydrate to give the most secretion, protein less, and fat the least Results in humans have been quite contradictory, but the most reliable bear out the findings derived from animal experiments There is a group of investigators that found carbohydrate to elicit the least secretion (5, 6) while another reported this type of diet to give the most abundant yield of pancreatic juice (7, 10, 23, 35) Among these reports one finds considerable variation in the diets used and also in most of them a significant amount of the other two food substances in the so called "pure diets" Holsti's conclusions are probably the most reliable and his results in brief are Carbohydrate yields the most abundant secretion of the pure food stuffs, protein less, and fat least About the secretion curves he says that the secretion after carbohydrate begins at once, is quite regular and during the observation period is quite active, reaching its maximum in 2 hours Proteins bring forth an initial rise after which the secretion falls to nothing until the middle of the second hour when it commences with considerable intensity and reaches its maximum in the third and fourth hours After fat (introduced by a tube) nothing happens before the third hour and then lasts only 1 hour

One author (35) concludes that the secretion curve after a mixed meal is a composite of those for the individual food constituents making up the meal

On the basis of his findings, Wohlgemuth introduced a low carbohydrate diet together with large amounts of sodium bicarbonate as an aid in bringing about closure of pancreatic fistulas In 1908 the same author wrote of several cases collected from the literature in which dramatic closure of the fistula had followed an institution of his so called anti-diabetic regimen The efficacy of such measures has been confirmed by some (6, 11, 22, 29) and denied by others (7, 17, 30)

2 *Chemistry* All investigators agree that pancreatic juice is alkaline and those who have investigated the question find the alkalinity to rise after meals (8, 9) Most authors have found pancreatic juice to be a clear, colorless liquid with small shreds of mucus, but there are notable exceptions where the pancreatic juice was observed to have a yellowish tinge at times (9, 19, 27, 29) In Table II is found a summary of the chemical results reported by the various investigators

TABLE III—SHOWING ENZYMATIC ACTIVITY

	After [illegible] fasting	After carbohydrate meal	After cream meal	After egg white meal	Normal duodenal contents (McClure et al)
Lipolytic action	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Amylolytic action	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Proteolytic action	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Proteolytic, plus antitrypsin	[illegible]	[illegible]	[illegible]	[illegible]	

Extracts from clots showed no appreciable proteolytic activity

All above figures represent determinations based on analyses outlined by McClure, Whitmore, and Reynolds (1)
The specimens were collected on the stated hour after the injection of the meal
All the above specimens were analyzed within 2 hours after taking
The figures on the lipolytic action indicate the activity measured in cubic centimeters of tenth normal sodium hydroxide developed in cotton seed emulsion by different specimens of [illegible] cubic centimeter of dilution of [illegible] pancreatic juice incubated for [illegible] hour at 40 degrees C
The figures on amylolytic action indicate the milligrams of sugar developed from soluble starch (44 per [illegible]) by various samples of [illegible] cubic centimeter of dilution [illegible] pancreatic juice incubated for [illegible] minutes at 40 degrees C
The figures on proteolytic action indicate the milligrams of new protein nitrogen developed from casein by various samples of [illegible] cubic centimeter of dilution [illegible] pancreatic juice incubated for [illegible] minutes at 40 degrees C

Glaessner and Popper found pancreatic juice to contain an active hemolysin for dog's corpuscles Wohlgemuth showed this to be an auto-hemolysin as well as a hetero-hemolysin. He thought it similar to the hemolysin of cobra and other venoms because like these it is activated by the presence of *lecithine*. *Glaessner and Popper* also showed that a subcutaneous injection of pancreatic juice into dogs had little effect whereas after an intraperitoneal injection of 8 cubic centimeters the dogs died within 5 hours

3 *Enzymes* All the cases of proved pancreatic fistula that we have been able to find showed active amylolytic and lipolytic enzymes when these were sought Both are increased in activity by bile and intestinal juice while the latter is augmented by liver juice and sodium taurocholate The majority of investigators are agreed that trypsin is secreted in inactive form and this fact explains the failure of pancreatic juice to digest the wound in many instances, for only with active trypsin is this effect noted (14, 19) That intestinal juice converts trypsinogen into active trypsin was first observed in humans by Glaessner (8) whose findings have been corroborated by a great number of observers There are many substances capable of activating trypsinogen and among them are 1 per cent hydrochloric acid, peptone bile liver liver extract and calcium chloride

Of importance in evaluating our results is that contact with air for 1 day (12) as well as that contact with bacteria and bacterial filtrates will also activate trypsinogen. Either of these factors may explain our results of finding active trypsin in our experiments, for no precautions were taken to assure sterile specimens and sometimes 12 hours elapsed before the analysis of enzymes was made.

Rennin or labferment has been found by some (12 35) and not so by others (8 9 27)

Another question in regard to enzymes is their quantitative relationship to the type of food taken The Pawlow School (25) has been staunch in defending the *Zweckmaessigkeits Prinzip* which holds there is increased lipase secreted in response to a fatty meal etc. As Pawlow says, "The work of the digestive glands is elastic to a high degree while it is at the same time characteristic, precise and purposive This elasticity has not been confirmed for the secretion of pancreatic juice in humans

Many observations have been made on humans with the purpose of determining enzymatic response to different types of food (7 8, 9 14 31 35) but the conclusions reached seem scarcely justified in view of the evidence presented Here again Holsti's work is exceptional because he used "pure diets" and had a well controlled series of experiments His conclusions were identical for diastase and lipase but the results with trypsin were inconclusive although here the method of analysis might lead to errors in results For lipase and diastase Holsti concludes (1) There

are secretions rich and poor in ferments given off by the pancreas (2) The concentration of enzymes is not dependent upon the rate of secretion (3) Nevertheless after the same meal in repeated experiments there is a definite relationship between speed of flow and the concentration of enzymes Although 2 and 3 may seem paradoxical at first reading one realizes on further study that for a given food there will always be a certain concentration of enzymes at a given speed of flow which may be quite different from that of another pure food or a mixed meal Babkin and Sawitsch (2) find the same true for animals and feel that there is a certain type of juice secreted for each food or mixed meal which is not determined by the speed of flow

4 *Pharmacology A Hydrochloric acid* Glaessner showed that a weak solution of hydrochloric acid stimulates pancreatic secretion which commences after a latent period of ½ hour and lasts ½ hour This has been confirmed by a number of authors (9, 12, 24, 35)

B Sodium bicarbonate Glaessner reported bicarbonate as having no effect on pancreatic secretion, but others have noted it as inhibiting the output (11, 15, 25, 40)

C Atropin This has a diminishing effect on secretion (8, 12, 29, 30)

D Pilocarpin In addition to its enhancing of the secretory state of the pancreas (12, 30) pilocarpin is reported as increasing the proteolytic power of the juice secreted (12)

E Water Holsti found that if water is given with the diet there is a different type of secretion curve than without water, but the total amounts are about the same Only when water is given with food in large amounts (60 cubic centimeters) does it increase pancreatic secretion above that elicited by the food alone

5 *Psychic secretion* The fact that there is an increased flow of pancreatic juice only a brief period after food is taken (in Holsti's case 1 minute after bread, cream, or gruel) has led many investigators to determine whether the pancreas is like the stomach in its response to psychic stimulation Negative results were reported by several authors Villaret and Justin-Besancon maintained their patient on a constant diet until he became anorexic, but this influenced the flow of pancreatic juice little when the same food was taken And when the diet was changed to a more agreeable fare and the patient salivated profusely, the output of pancreatic juice was not increased for 40 minutes even when the patient chewed but did not swallow the food Similar results were noted by others (7, 14)

Holsti believes that there is a psychic secretion, but his basis for this rests upon an erroneous interpretation of facts None of his results which cannot be explained by the secondary stimulation by hydrochloric acid of pancreatic secretion

After reviewing the experiments it seems justified to conclude that if there is any psychic secretion it is only very slight

6 *Diabetes and pancreatic fistulas* Several investigators have noted that a diminished sugar tolerance obtains in cases with pancreatic fistula (7, 12, 22, 23) Holsti and Monat noted that this returned to normal when the fistula cleared up

SUGGESTIONS FOR FUTURE STUDY

Cases similar to the one reported in this paper as well as those summarized from the literature are quite uncommon We therefore take the liberty to suggest that future studies may possibly be directed toward solving the following

The effects of rennin or labferment

The *Zweckmaessigkeits Prinzip* of Pawlow as it might be applied to humans over a long period of time

The enzymatic content whether proportional to solid content of pancreatic juice?

The use of Holsti's meals as a standard for test diets

The estimation of enzymes by Willstatter technique

The collection of all specimens of pancreatic juice in sterile bottles with immediate chemical and enzymatic studies

SUMMARY

A case is reported with an intubation of Wirsung's duct following successful resection for cancer of the ampulla of Vater The largest amount of pancreatic juice obtained in 24 hours was 1,384 cubic centimeters

Volumetric curves for the digestive phase of pancreatic activity are given Pancreatic secretion is constant Of the pure food meals given only glucose gave reliable results.

Ether and atropin inhibit. Pilocarpin, physostigmine, and water by mouth under certain circumstances stimulate pancreatic secretion.

The physical properties and some chemical analyses of pancreatic juice are given

Figures for enzymatic content of pancreatic juice are recorded for fasting specimens and those obtained after meals with major portion of one foodstuff. They are not sufficiently numerous to be conclusive All three enzymes were found in high concentration in all specimens of pancreatic juice obtained

A review of some pancreatic fistulas as reported in the literature is presented

Recommendations for further study on human pancreatic fistulas are made

We wish to thank Dr Beth Vincent for the use of his case and to acknowledge our indebtedness to Dr E D Churchill and Dr Chester Jones for their criticisms and suggestions

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PHYSIOLOGICAL CHANGES IN THE URETER ASSOCIATED WITH PREGNANCY[1]

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ANATOMICAL changes in the ureter of the pregnant woman have been a subject of study since 1843 when Cruveilhier first described the dilatation and elongation of the ureter as a frequent accompaniment of the gravid state We have learned that there is a hyperplasia of the tissues composing the walls of the kidney pelvis, the ureter, and the bladder in the form of increased thickness of the muscular and connective tissue elements In addition, there is elongation of the ureter and dilatation of the ureter and kidney pelvis The extent to which these changes take place varies much in different individuals, as well as in the two tracts of the same individual, the process usually being more marked upon the right side

Two schools of thought have arisen as the result of prolonged attempts to explain this phenomenon The first and older group has felt that pressure of the enlarged uterus upon the ureters, particularly at those points where the ureter crosses the pelvic brim, was the chief factor In addition, it has emphasized the frequent dextro-rotation of the uterus as well as the prominent relationships of the large iliac vessels on the right to account for the greater degree of dilatation and elongation usually observed in the right tract The other school has felt that these anatomical relationships were undoubtedly factors of importance but could not be accepted as the complete explanation, pointing out that larger pelvic tumors than those represented by the pregnant uterus, such as myomas and ovarian cysts, were not often productive of the ureteral changes in the non-pregnant individual In addition, dilatation of the ureter usually reaches its maximum at about the seventh month of pregnancy, and frequently diminishes toward term, despite the constant enlargement and increasing weight of the uterus For these reasons, it has been maintained that some other factor than the enlargement of the uterus must exist Several writers have suggested an atony of the ureteral musculature, however, thus far no one has succeeded in proving atonia to exist although various attempts have been made to do so Until recently, these have consisted in observing the relative frequency of spurts of colored urine as they emerged from the ureteral orifice into the bladder These studies have seemed to indicate a definite decrease in the muscular activity of the ureter in pregnancy, but have not been conclusive in that the periods of observation were necessarily short and were not carried out on the same individuals at different stages of pregnancy, so that one could not be sure that the differences noted were not individual variations

The practical importance of the problem lies chiefly in the relationships of these ureteral dilatations to the incidence of urinary stasis and subsequent infections Indeed, it would seem to be the most important single factor in explaining the incidence of pyelitis in pregnancy

Trattner and his associates have perfected an apparatus which makes it possible to observe and record the peristaltic activity of the human kidney pelvis and ureter Their application of this device has been confined to the ureter of the male and the non-pregnant female In this study, we have used the Trattner hydrophorograph, as he has named the device The apparatus consists essentially of a tambour lever and water manometer connected through a two-way stopcock to an intra-ureteral catheter and is equipped with an adjustable escape valve An electrical counting device records simultaneously the rate of urinary excretion (Fig 1) By means of an adjustable escape valve, any level of intra-ureteral tension can be maintained or varied at will The apparatus is equipped with a recording device which produces a permanent record that can be preserved and

[1]Submitted for publication April 1, 1935

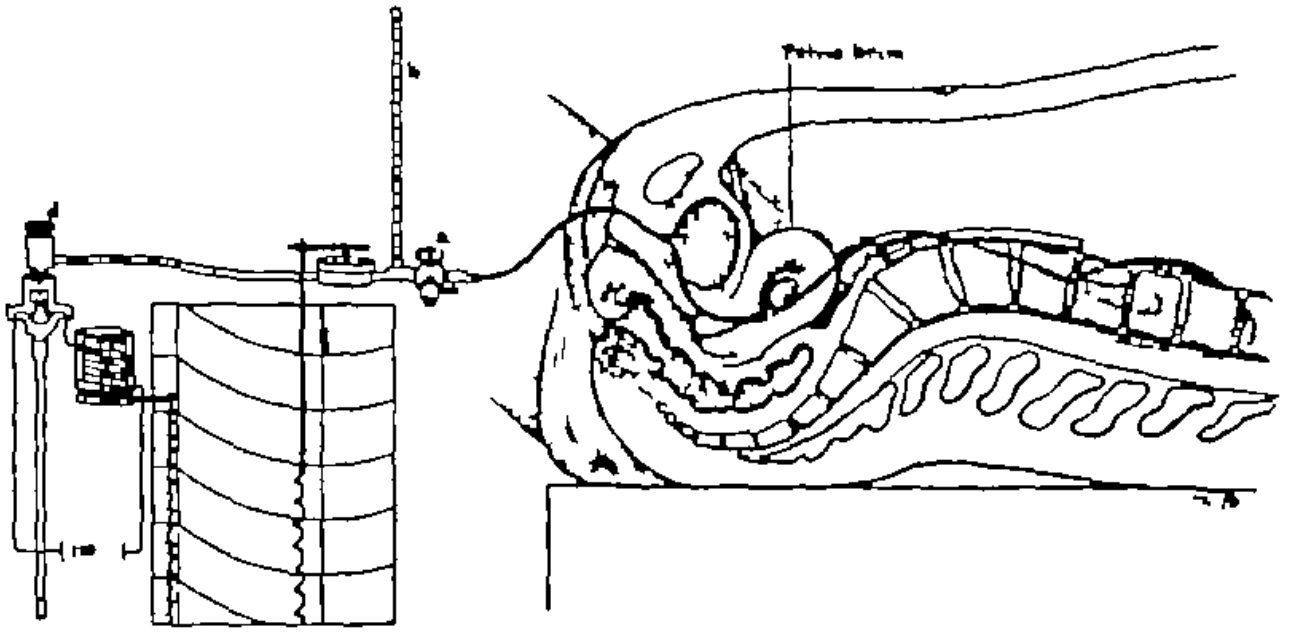

Fig Diagrammatic drawing illustrating the principle of the hydrophorograph a, three-way stopcock, b water manometer connected with the ureteral catheter and tambour providing visual means of checking pressure levels as well as amplitude of fluid waves resulting from peristalsis, c, tambour and writing lever d, adjustable escape valve providing means for controlling intra-ureteral pressure e, electrical drop counting device

makes possible a comparison of ureteral activity

Thus far we have studied 34 women 27 of whom were pregnant or puerperal, and 7 normal non-pregnant controls. The relationship of the observations to the various stages of pregnancy are expressed in the accompanying table (Fig. 2)

It has been possible for us to make repeated observations at monthly intervals on 12 of the 27 pregnant women whose ureters were studied All of the deductions that have been made concerning variations in the physiological activity of the ureter in the different periods of pregnancy are based upon the study of this group of patients. The remaining 15 upon whom one observation or at the most, two were possible, have been used cautiously because of the variation that exists between individuals For the most part, they were found to conform to the characteristics of the various types of curves and their incidence in pregnancy as established by the more intensively studied group and therefore, they have been included in this report as cumulative evidence.

Each time a hydrophorograph record was taken a retrograde pyelogram was made with the injected contrast medium under as nearly the same pressure as possible The object in

	Non Pregnancy	PREGNANCY			Postpartum
		1st Trimester	2d Trimester	3rd Trimester	
Normal curve	(7)	(3)	(8)	(5)	1
Modified curve		1	(3)	(3)	1
Flat curve		1	(3)	1	(1)

Fig 2 Indicating the number and distribution of observations of normal, modified and absent ureteral response

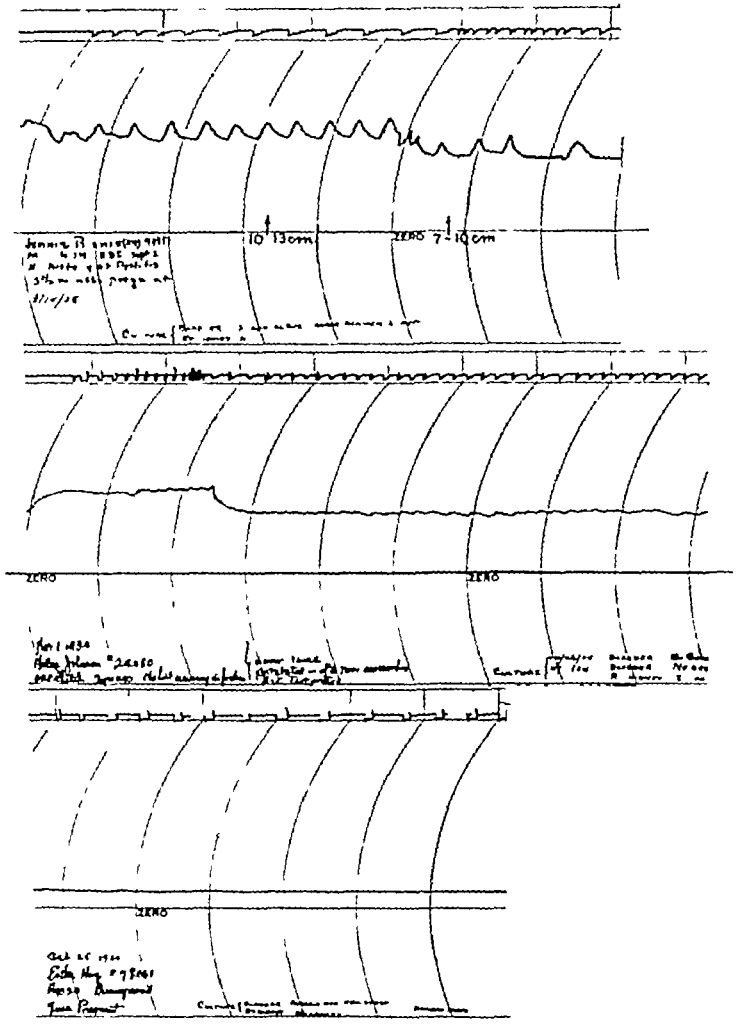

Fig 3 Actual ureteral tracings illustrating normal, modified, and absent response

making the roentgenogram was to ascertain the relationship between dilatation of the ureter and loss of peristaltic activity on the one hand, and, on the other, to control accurately the distance the catheter was allowed to ascend the ureteral tract The upper end of the catheter was kept as nearly as possible at the upper margin of the pelvic brim In this way, we have compared that portion of the ureter lying above the pelvic brim in all patients whether in late or early pregnancy Wislocki and O'Connor showed in their ureteral experiments upon dogs that activity of the organ depended upon, and varied tremendously with, the rate of urinary secretion In other words, it is necessary to provide the ureter with an adequate mass to propel Therefore, we have made certain that all our patients ingested large amounts of water during the hour preceding an observation and have attempted in this way to obviate a source of possible error

After catheterizing the right ureter, the catheter was immediately connected with the hydrophorograph and a record made of the rate of urinary excretion simultaneously with

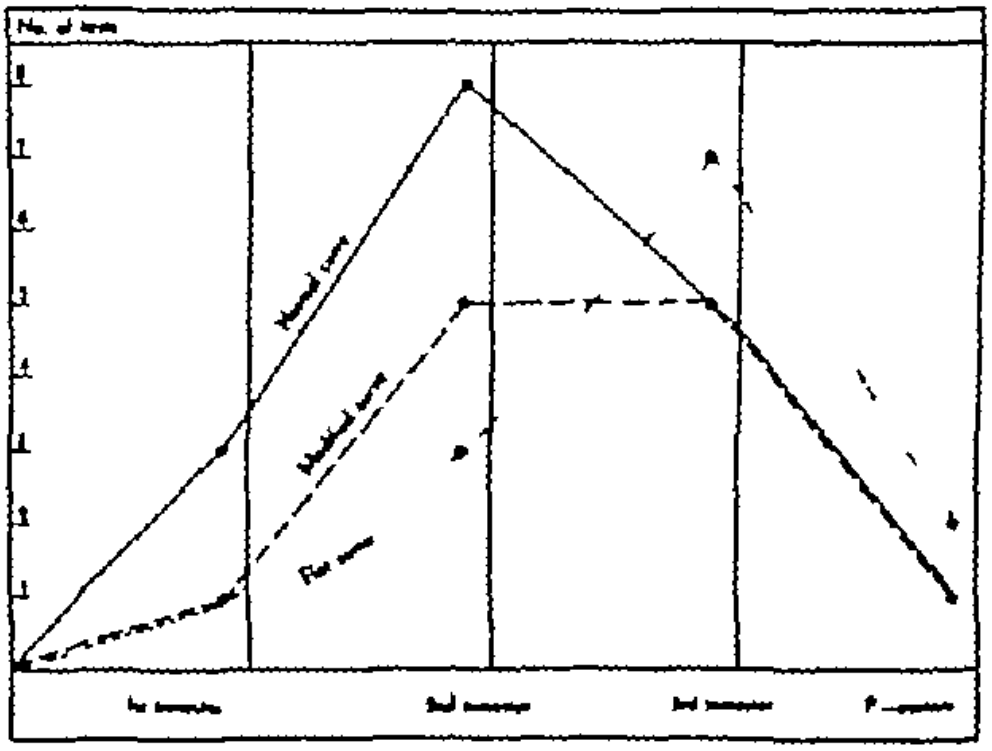

Fig 4 A graphic representation of the data contained in Figure 2, including the non-pregnant group, showing the incidence of normal and modified response with respect to the various trimesters of pregnancy

one of the peristaltic pattern of the ureter We found that the ureter response varied with the intra-ureteral pressure, that of the normal non-pregnant individual being maximal at pressures lying between 4 centimeters and 12 *centimeters of water pressure* For the purposes of our study we commenced at a pressure slightly higher namely 15 centimeters of water pressure and then dropped this by successive stages to 10 centimeters and 5 centimeters, maintaining each level for approximately 3 minutes and recording the ureteral response at each level. In this manner we have hoped to offer the optimum conditions for muscular response in each case.

Months of pregnancy									
	1st	2nd	3rd	4th	5th	6th	7th	8th	9th
Normal curve		I	II	IIII	II	II	II	II	I
Modified curve			I	II	I	II	II	II	I
Flat curve			I		I	II	III	III	I

Fig 5 The distribution of the three types of ureteral curves with respect to the various months of pregnancy

The presence of urinary tract infections has been ruled out by taking ureteral and bladder urine cultures at the time each observation was made *This seemed important* as it has been demonstrated that during the acute phase of an infection, peristaltic activity may be increased, whereas during the chronic phase, it may be depressed or absent. All patients included in this study had consistently negative ureteral bacterial cultures.

As will be seen from a study of the graphs, we observed three general types of variation *in the peristaltic record* *The first is a regular* rhythmic curve of fairly uniform amplitude of excursion at all levels of pressure this is considered normal The second shows a lesser degree of excursion with a greater response, usually at one level or another as well as irregularity in the degree of excursion this group we have characterized as modified response and have found it to be frequent in the *earlier months of pregnancy* *The third is* characterized by a total lack of rhythmic muscular contraction at any level and has been found to be a frequent observation in

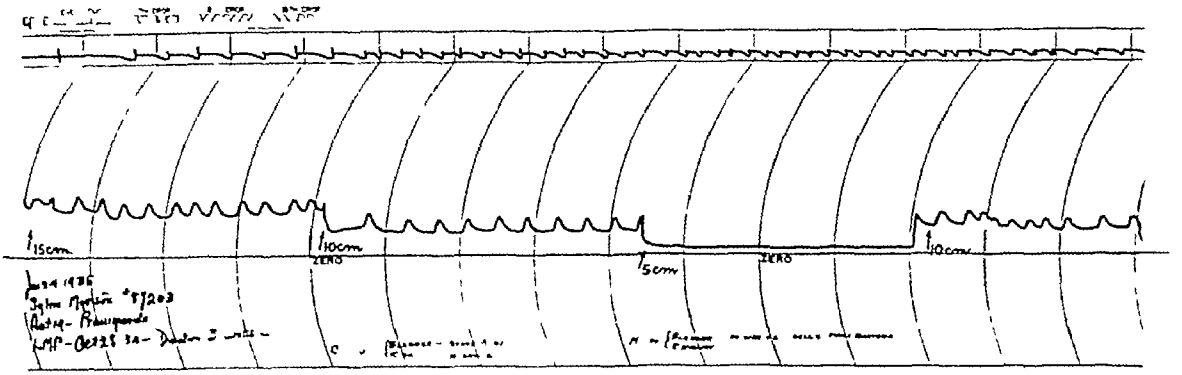

Fig 6 Ureteral tracing—third month of pregnancy, showing normal response at a higher pressure level and lack of response at 5 centimeters

the latter months of pregnancy (Fig 3) The incidence of these three types of response with respect to the various periods of pregnancy are portrayed graphically in Figures 4 and 5.

From this, it will be seen that, during the first and second months of pregnancy, ureteral activity is quite normal With the passage of the third and fourth months, the incidence of modified ureteral response becomes more marked, whereas during the sixth, seventh, and eighth, modified response or total lack of response becomes the rule During the ninth month, there is evidence of a returning irritability in the form of more adequate muscular activity

The foregoing statement is the result of our experience in most instances However, not all patients show diminished peristalsis as indicated A small minority (2 in our whole series of 34 cases) maintained normal ureteral activity throughout pregnancy (Fig 5)

The most constant early change observed was the disappearance of peristalsis when 5 centimeters of water pressure was maintained within the ureter, after the ureter had responded well at the higher levels of 10 centimeters and 15 centimeters This observation seems to hold good regardless of the degree of ureteral dilatation and also the rate of urinary secretion (Fig 6)

We have given a great deal of thought to the possible causes of this variation in the ureteral peristaltic activity associated with the various phases of pregnancy It is well known that slight distention of a hollow viscus capable of peristalsis, stimulates that organ to increased activity, whereas overdistention obliterates its power of rhythmic contraction for a time, but there will be a return of this property provided the distention has not been excessive and has not persisted for too great a period of time For this reason, we have

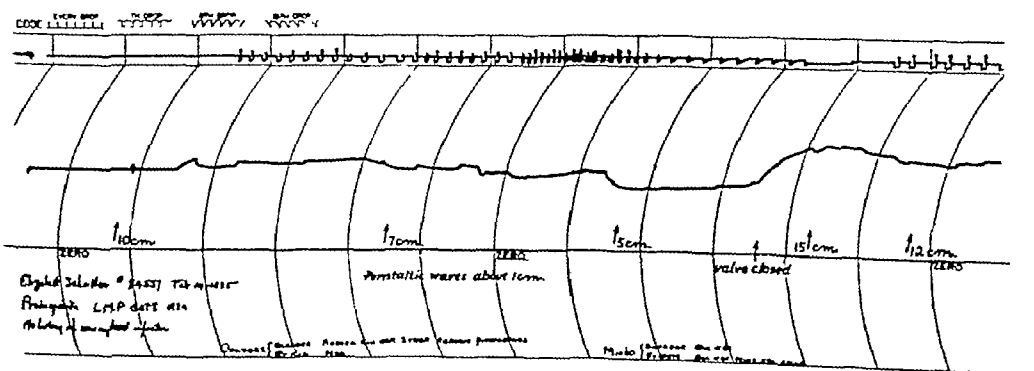

Fig 7 Tracing at fourth month of pregnancy showing markedly modified peristalsis even though the secretion of urine (24 drops per minute) is rapid

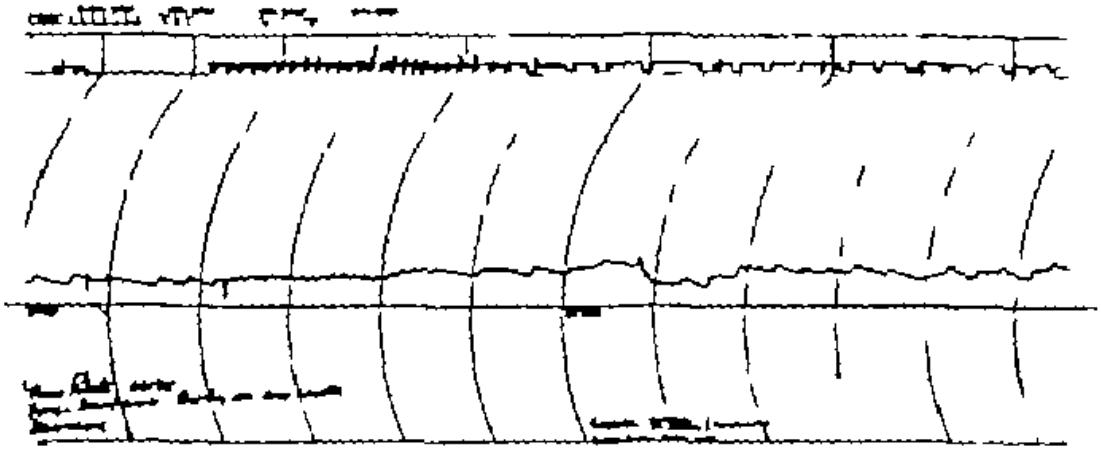

Fig 8 Tracing taken during the seventh month of pregnancy demonstrating modified muscular activity with rapid excretory ability in a widely dilated ureter

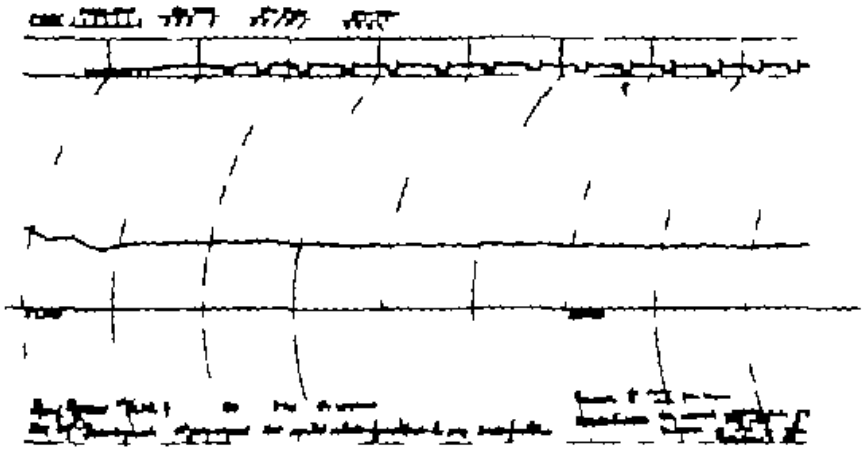

Fig 9 Eighth month of pregnancy showing completely atonic ureter Not excretion of urine in 8 drops per minute

studied the pyelograms of these ureters hoping that there might be a close parallelism between dilatation of the ureter as an expression of prolonged distention and the incidence of modified or absent peristalsis. Thus far we have failed to find any such relationship particularly during the second, third fourth, and fifth months of pregnancy when the process is supposedly in its incipiency The degrees of dilatation observed as a concomitant of normal pregnancy may or may not be associated with loss of peristaltic activity

A few instances have been observed in which very widely dilated ureters were possessed of normal muscular activity (Fig 8) We are therefore, forced to the conclusion that the weight of the enlarged uterus upon the ureters with embarrassment of urinary outflow and subsequent dilatation, is associated with loss of muscular activity in varying degree but is not its cause. The observation that there is at least a partial return of peristalsis during the ninth month (Fig. 10) is final convincing proof of the correctness of this opinion. One is forced to conclude that there must be another cause of atony of the ureter in pregnancy and that the loss of muscle tone is contributory to the dilatation of the ureter rather than the reverse.

Inasmuch as we know little concerning the possible causes of ureteral atony in the pregnant woman it may be of profit to apply speculatively some of the facts that have been gleaned concerning other organs the walls of which are composed mainly of smooth muscle. For example Westphal has demonstrated a marked diminution in the muscular irritability of the gall bladder in pregnancy Hofbauer pursuing this line of investigation demonstrated that hypertonic solutions of cholesterin

salts produced this effect and argued that inasmuch as the blood of the pregnant woman contained markedly increased amounts of these salts, this was a possible explanation of the phenomenon

The large bowel is another structure of the body which has been demonstrated to undergo marked regression of its muscular response during pregnancy. This observation has long been invoked as the explanation of the constipation experienced commonly during the latter months of pregnancy, but thus far no more rational etiological factor has been advanced than that of the weight of the pregnant uterus, which, in view of our studies on the ureter, does not appear to be an adequate explanation

The outstanding example of smooth muscle atony of a hollow viscus in pregnancy is, of course, the uterus In this organ loss of muscular irritability is the most important single factor in insuring the successful fruition of pregnancy. Knaus has shown rather conclusively that one substance capable of producing this effect on the uterus is the hormone of the corpus luteum, progestin Whether this is the only substance instrumental, or even the most important one, seems doubtful, because we know that removal of the corpus luteum from the body of the pregnant woman after the third month is not accompanied by a prompt return of contractility on the part of the uterus, with resulting abortion

It would seem likely that the body had been provided with a superabundance of some substance capable of producing atony in smooth muscle for the purpose of safeguarding pregnancy and that its effect is not entirely specific for uterine musculature but, in addition, possesses a modified, though similar, action upon other structures At this time, we must content ourselves with speculation upon the subject, though we hope at some future time not only to present a more complete picture of the effect of this phenomenon but, in addition, to offer some evidence as to its nature and mode of action

CONCLUSIONS

1 The normal ureter of the non-pregnant woman is possessed of rhythmic peristaltic activity which can be measured and recorded

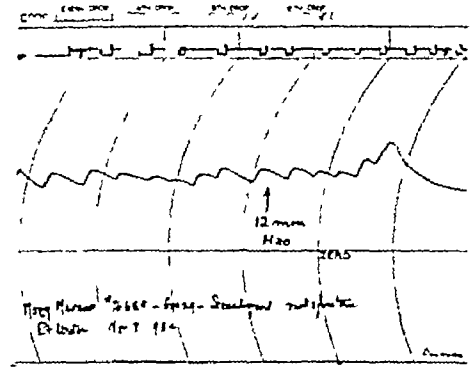

Fig 10 Tracing of same ureter as illustrated in Figure 9, one month later (ninth month) demonstrating a remarkable return of ureteral activity

2 This rhythmic peristaltic activity is definitely altered by pregnancy in varying degrees in the majority of our patients (34) studied

3 This altered peristaltic activity is expressed by diminished amplitude of the peristaltic wave, commencing in the third month of pregnancy, but reaching its peak during the seventh and eighth months

4 After the fifth month the number of patients showing diminished ureteral response exceeds those showing normal activity

5 During the last month of pregnancy there seems to be a definite return of muscular irritability as expressed by the measurement of peristalsis and response to stimulation

6 This diminished peristaltic activity of the ureters seen in pregnancy cannot be explained on a basis of dilatation On the contrary, dilatation of the ureters during pregnancy is probably in great part dependent upon the atony of the ureters

7 The etiology of this observed ureteral atony during pregnancy is, in our opinion not dependent upon any mechanical factor but rather upon some, as yet unexplained, chemical basis

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Figs 5 and 6 Loss of right ala Restoration by skin flap from side of nose Less secondary scarring is produced by method illustrated in Figures 19-21

denuded. The skin provided has a color and texture which differs markedly from that of the facial integument The presence also of large amounts of subcutaneous fat interferes with molding and, according to some, with proper healing as well The necessarily prolonged maintenance of the arm before the nose during the grafting period is a source of great discomfort to the patient and is not without danger of permanent arm damage through subsequent contractures.

To be acceptable, a surgically reconstructed nose must have a covering of smooth skin of normal color a contour which harmonizes with the face a functional epithelial lining, and an adequate airway Infectious or malignant processes must be eradicated before repair is commenced distorted tissues must be freed and replaced. In the plastic reconstruction each damaged or missing component and anatomical structure (lining, covering and supporting framework) must be restored The ideal toward which the surgeon must strive is complete anatomical and physiological restoration with a minimum of residual or secondary scarring

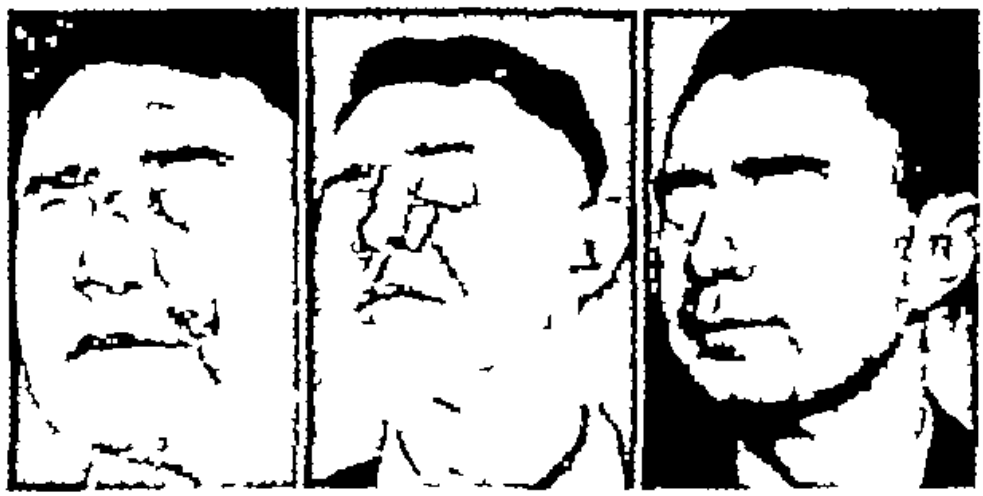
For reconstructions about the nasal tip, the author makes use of the following methods, the choice being determined by the nature and extent of the lesion (dermal, soft tissue, or supporting structure defects)

SKIN AND SOFT TISSUE DEFECTS

1 *Small skin defects* are readily covered by Wolfe grafts obtained from the upper eyelid or posterior aspect of the ear This method is particularly useful when repair of surface skin defects is attempted shortly after injury (Figs 1-4)

2 *Defects of the ala nasi* may be corrected by delayed pedicle flaps rolled down from the side of the nose, the normally rounded alar border being formed by the rolled edge The resulting defect at the side of the nose is then covered by a Wolfe graft (Smith) This method is best reserved for small lesions (Figs 5-6) Restoration of the base of the ala may also be accomplished by delayed pedicle transfers from the region of the nasolabial folds (Figs 7-9) A slight though nevertheless visible facial scar is the only objection to this method

3 *Skin and soft tissue losses at the nasal tip in women* especially when extensive, are best treated



Figs 7 8, 9 Loss of left ala, distortion of nasal tip and partial obstruction of nostril Correction by means of pedicle graft from left nasolabial fold Nasal lining formed by invaginating tip of graft into the nostril The scar in the nasolabial fold is scarcely visible

Figs 10, 11, 12 Loss of nasal tip in motor accident. Restoration by forehead flap nourished by left temporal artery The forehead scar after Wolfe grafting is concealed by the hair dress

Figs 13, 14, 15 Nasal amputation to remove carcinoma of the nasal tip Reconstruction of nose 1 year later by Indian method Secondary forehead scar after Wolfe grafting concealed by hair dress

Figs 16, 17, 18 Loss of skin over bridge, tip, and alæ Author's method for restoring nasal skin in males Unsightly forehead scars are avoided

Figs 9 to 2 Loss of right ala as result of dog bite Restoration by notice method Nasal lining provided by inverting the distal portion of the flap

by forehead flap transfers either by pedicles nourished by the temporal artery (Figs 10–12) or by the classical Indian method (Figs 13–15) The axis of the flap and its situation on the forehead should be determined by the location and extent of the lesion as well as by the patient's style of hair dress A nasal lining is provided from the skin surrounding the defect or by the application of Wolfe grafts to the under surface of the forehead flap before its transfer to the nose. The forehead scar which remains after Wolfe grafting is concealed by the hair

The disadvantage of this method in men lies in the inability except in unusual cases, to conceal the forehead scar by the hair To avoid these unsightly scars in men, the author has devised a method of rhinoplasty by means of which, skin from below the ear may be transferred to the nose on a tube pedicle via the sternal notch Since its original publication,[1] the author has performed this operation successfully in several additional cases with very gratifying results. This method has several distinct advantages (1) forehead scars are avoided (2) the skin matches the nasal integument and is practically hairless, (3) the skin is thin and easily molded to shape (4) the resulting neck scar is inconspicuous (Figs 16–21)

SUPPORTING STRUCTURAL DEFECTS

In cases requiring reconstruction of the cartilaginous portion of the nasal bridge use

See A the plastic surg 1 August 1911

Figs and 3 Defect in nasal bridge resulting from septal abscess following bite sting Depression filled in by insertion of pieces of ear cartilage through nasal columella incisions

Figs 24 and Depression of cartilaginous bridge and nasal tip resulting from fall in infancy Correction of this deformity as obtained by inserting hinged rib cartilage transplant

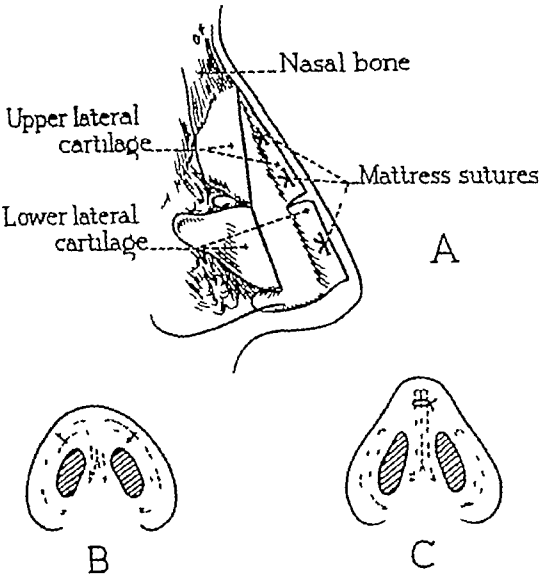


Fig 26 *A*, Diagram illustrating author's method for raising nasal bridge by everting upper lateral cartilage flaps *B* and *C* Diagram illustrating Kazanjian method of raising and narrowing nasal tip by using flaps of alar cartilage The author combines this procedure with *A* to correct depressions of the nasal tip and bridge

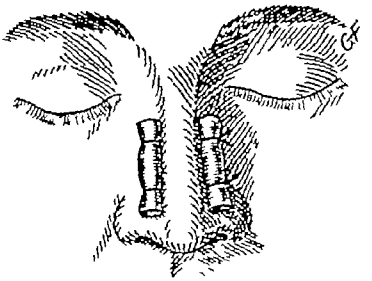


Fig 27 Illustrating author's method of maintaining upright position of newly formed cartilaginous bridge by means of mattress sutures of horsehair passed through the cartilage flaps and tied over gauze rolls for one week.

should always be made of cartilage rather than prosthetic inserts of foreign substances (ivory, etc) Cartilage is not absorbed and has the advantage of being readily shaped and easily grafted The cartilage can be obtained from several sources, the choice of which is determined by the nature and extent of the defect

1 *Depressions of the cartilaginous bridge* associated with prominence of the nasal tip can be filled in by one or more pieces of ear cartilage inserted through a mid-columellar incision (Figs 22–23)

2 *Broadly depressed cartilaginous bridges* associated with overhanging flattened nasal tips can be treated by several methods

A Hinged or mortise-jointed rib cartilage transplants may be inserted so that the vertical support rests upon the maxilla, the horizontal arm is shaped to correct the defect in the nasal bridge (Figs 24–25)

B The introduction of rib cartilage transplants for depressions of the cartilaginous bridge can be avoided by the use of the author's recent extension of the principle of the Kazanjian operation (eversion of the lateral wings of the alar cartilage and suturing them back to back to support the nasal tip) The author augments this procedure by including also the upper lateral cartilages

Figs 28 and 29 Early childhood injury resulting in flattened nasal tip and bridge Front view showing nose before and after correction by author's method (see Figs 26 and 27)

Figs 30 and 31 Profile view of preceding case showing broad drooping nasal tip Shortening of nose, elevation and narrowing of nasal tip and bridge accomplished in one operation (Author's method)

which are first cut, according to the depth of the bridge depression and then everted. They are next stitched back to back with two sutures of chromic catgut. Horsehair mattress sutures passed through the everted cartilage flaps and tied over rolls of gauze help to maintain their upright position (Figs. 26–27). The horsehair sutures are removed in 1 week.

This method combined with that of the Karanjan operation (which merely elevates and narrows the nasal tip) has produced excellent corrections of overhanging flattened nasal tips associated with broadly depressed cartilaginous bridges. It has the advantage of eliminating the necessity of rib resections as a source of cartilage, a disabling procedure which is not devoid of danger. It also forms a more flexible and natural nasal bridge than is obtained from the use of rib cartilage transplants. Moreover the advantage of permitting the surgeon to shorten the nose and to elevate the bridge in a single stage operation without the necessity of external incisions, represents a distinct advantage over the more complicated and hazardous procedures hitherto described. The absence of a nasal septum strong enough to support the everted cartilages is an important contra indication to this procedure (Figs. 28–31).

SUMMARY

1. The correction of deformities about the nasal tip demands carefully individualized management if ideal results are to be attained. The operation should be adapted to the patient, not the patient to the operation.

2. Operations providing facial skin and a minimum of secondary deformity are most desirable.

3. The author describes his method for restoration of the nasal tip and his technique for correction of bridge defects by means of upper lateral cartilage flaps.

MALUNITED FRACTURES AFFECTING THE ANKLE JOINT

With Special Reference to Twenty-two Cases Treated by Arthrodesis

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MANY ankle joints of which the anatomy and function have been disturbed by fractures continue to give symptoms long after the fracture has healed To insure a symptomless ankle one must obtain union of the fracture with complete reposition of the talus directly under the axis of weight bearing and anatomical restitution of the joint topography

The writer has reviewed the records of all of the 216 patients who entered the New York Orthopædic Dispensary and Hospital during the years 1928 to 1933, inclusive, with malunited fractures affecting the ankle joint These patients, with four exceptions, had their initial treatment elsewhere, but because of continued symptoms had looked to other sources for relief The lapse of time since fracture ranged from a few weeks to many years, in most instances more than 6 months

Failure to secure and retain complete reduction had resulted in symptoms varying from a dull ache present only at weather changes to a constantly painful ankle causing the patient to walk with a protective limp and to resort to a cane or crutch Physical findings varied from the apparent normal to a greatly swollen, cyanotic ankle and foot with limited and painful motion, tenderness over the fracture sites and anterior surface of the joint, and distortion of the ankle mortise In the latter, dorsiflexion was often greatly limited, so that the patient either bore weight on the forefoot only or, to get the heel to the ground, hyperextended the knee and externally rotated and abducted the hip

Eighty-eight per cent of the fractures had occurred in adults, of these 71 per cent were in females, whereas among those under 18 years of age boys predominated over girls in the ratio of five to four The more common occurrence in women is too great to be ignored, especially since men are more subject to traumatic injuries This may be due to ankle instability incident to wearing high heels

NON-OPERATIVE TREATMENT

These patients were usually treated by means of a metal or rubber plantar arch, exercises, contrast baths, and massage Occasionally such measures as an inner heel wedge, ace bandage, adhesive strapping, and baking were used Salicylates were sometimes given for relief from pain and for the obese a reduction diet prescribed

Of these measures none helped more than a metal arch patterned on a plaster mold of the foot Patients with slight distortion of the joint sometimes obtained complete relief, especially if but a few weeks had elapsed since the injury and symptoms were partially the result of initial trauma to soft tissues and prolonged immobilization However, where distortion was extreme or arthritis present, relief was not complete and that which was obtained usually ended with cessation of treatment Patients having a history of previous foot strain or evidence of arthritis elsewhere, other factors being equal, responded more slowly to treatment

SURGICAL TREATMENT

Open correction of faulty union is widely practised but accurate reduction is difficult Its usefulness is limited to the early period following fracture before osteoarthritic changes have taken place None of the patients in this group came under our care sufficiently soon after their initial injury to warrant an open reduction

In 1608, Fabrig performed the first astragalectomy on record for fracture of the talus A successful result was reported This operation is still performed by some surgeons, especially in fractures of the talus entering both ankle and subtalar joints Sir Robert Jones stated "Total astragalectomy is a very much overrated operation, and its functional results disappointing, even though, as Whitman insists, the foot at operation be thrust well backward on the leg, it can, perhaps, give no worse functional result than leaving a permanently crushed astragalus" The writer is of the opinion that this operation is not indicated in fractures of the talus, for in every situation subtalar triple arthrodesis or ankle fusion, or the two combined, can be used to better advantage

Supramalleolar osteotomy may be used to correct the axis of weight bearing but does not change a deformity of the ankle mortise In children in whom a fracture has produced a disabling deformity by disturbing growth in a portion of

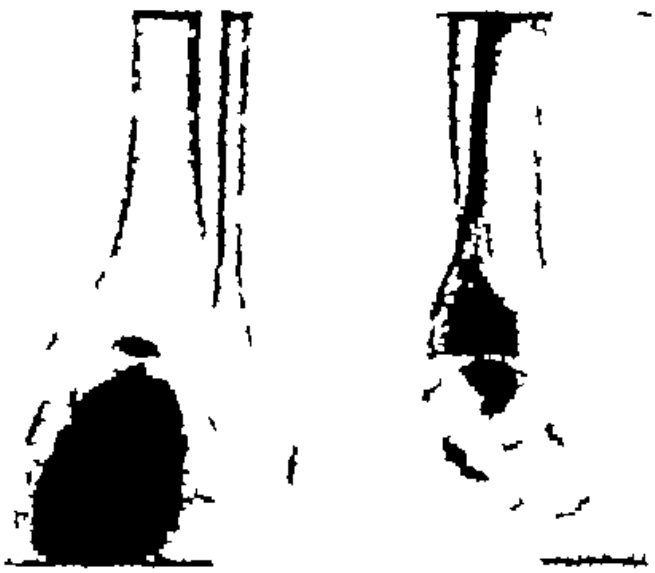

Fig. Six weeks after fracture passing through the medial portion of the distal tibial epiphysis and growth disc in a girl of 9 years. Anteroposterior and lateral views.

the lower tibial epiphysis, correction may be obtained and the deforming factor removed by excising the remaining portion of the epiphyseal line together with a sufficient wedge of bone to permit realinement of the tibia and ankle (Figs. 1, 2, and 3). This procedure should be accompanied by obliteration of the lower epiphyseal line of the fibula. In younger children an excresis of the corresponding growth disc of the opposite extremity is at times indicated (8). If shortening of the limb having the fracture exists, its growth can be stimulated by drilling the metaphysis in the region of the remaining epiphyseal lines according to the method described by Ferguson.

A calcaneal tendon lengthening combined with open correction of the fracture or ankle fusion may prove advantageous, but alone serves only to correct equinus. In this series, it was performed four times in combination with an ankle fusion.

Subtalar triple arthrodesis may be required if any one of these joints be entered by the fracture. It has been performed, we believe unwisely, as a means of correcting the lateral displacement of the foot, leaving the damaged ankle joint untouched.

An ununited malleolar tip may be excised when it is a source of pain, provided its absence will not cause instability of the talus in its mortise. One patient in this series had had symptoms for 10 years from three loose bodies involving the lower third of the medial malleolus. They impinged against an osteophytic spur on the talus. Removal of the loose bodies gave complete relief and there had been no recurrence of symptoms 20 months after operation.

By far the most useful surgical measure for a malunited fracture entering the ankle in which osteoarthritis has manifested itself or in which disruption of the joint is so extreme that its eventual presence is inevitable is ankle fusion. Of the 216 patients studied there were 58 in whom the writer felt that better function could be obtained and symptoms lessened by arthrodesis. This operation was done in 24 patients and in 22 sufficient time has elapsed to give one a fair idea of the end result to be expected.

ANKLE ARTHRODESIS

The ankle joint was first arthrodesed by Albert, in 1878, to correct a paralytic pes equinus. The operation became widely used and met with varying success. Later it replaced resection and amputation as a surgical means of treating tuberculosis. I have been unable to discover who first used arthrodesis to eliminate disabilities caused by distortion of the ankle mortise secondary to fractures. Apparently it is an old procedure which has been used by many surgeons in many countries as a last resort for the hopelessly shattered ankle. Sir Robert Jones advocated it during the World War as a means of treating severe gunshot wounds of the ankle, painful fibrous ankylosis and bony ankylosis in malposition. Since 1927 several references to it have been made in the literature, particularly in Great Britain. References have been in the form of a paragraph or two of generalizations with, to the writer's knowledge, no published detailed end-result study.

At least sixteen methods of arthrodesing the ankle have been described in the literature and much is made of the difficulty of obtaining osseous union. Of the 22 cases listed in this study definite osseous union was obtained in 21 and in the remaining case it is doubtfully present. Essentially the same procedure has been used at the New York Orthopedic Dispensary and Hospital with equal success to arthrodese a much larger series of unstable ankles resulting from anterior poliomyelitis. Previous statistics on arthrodesis for malunited fractures affecting the ankle have not been available, but Vulpius reported osseous union in 50 to 60 per cent and firm fibrous union in 20 to 25 per cent of his cases fused for instability due to anterior poliomyelitis.

The difficulty of securing osseous union and the danger of damaging the distal tibial epiphyseal line in performing ankle fusions before adolescence is much stressed by many writers, yet we do not consider youth an absolute contra-indication. We have obtained osseous union by arthrodesis in a tuberculous ankle of a child of 3 years without

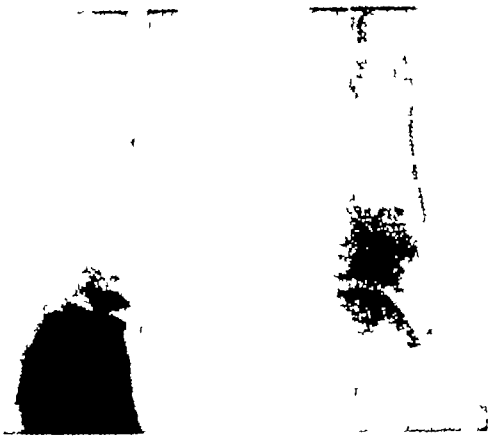

Fig. 2. Anteroposterior and lateral views of the same ankle as in Figure 1, 2 years later, showing varus deformity resulting from deficient growth of the medial portion of the distal tibial epiphysis.

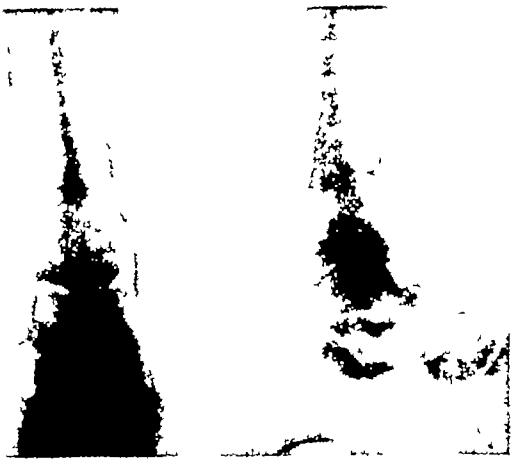

Fig. 3. Anteroposterior and lateral views of the same ankle as in Figures 2 and 3, 6 months after an excresis of the distal tibial and fibular epiphyseal lines together with a bone wedge sufficient to correct the deformity. Clinical result excellent. Metaphyses adjacent to other epiphyseal lines of this extremity drilled to stimulate growth. The patient is to be kept under observation and an excresis of the corresponding epiphyseal lines of the opposite extremity done if more than one half inch shortening results.

disturbing growth of the distal tibial epiphysis. The youngest patient in this series, aged 7, showed definite fusion in 3 months, and has been followed for 5½ years without evidence of disturbance of his epiphyseal growth due to the operation.

The degree of equinus in which an ankle is arthrodesed is of very great importance. Sir Robert Jones believed that an ankle should be fused so that the foot can dorsiflex a few more degrees than a right angle. Most writers on this subject prefer a few degrees of equinus.

In normal walking without shoes the foot is held in a calcaneal position as it is swung forward. When weight is borne upon the foot the heel does not leave the ground until the knee is well over the fore part of the foot, i.e., till the foot is dorsiflexed to considerably beyond a right angle. However, in many adults, particularly women, a contracted calf muscle prevents dorsiflexion of the foot even to a right angle, yet they may present what appears to be a normal barefoot gait except for early heel rising.

An ankle that is arthrodesed so that maximum dorsiflexion of the foot is from 100 to 90 degrees will permit an essentially normal barefoot gait. A foot in more than 10 degrees of fixed equinus gives a noticeably abnormal gait which becomes rapidly more awkward as equinus is increased until the heel either does not reach the ground or is brought to the ground by externally rotating and abducting the hip and hyperextending the knee. Not only is walking in this position difficult and awkward, but often it is accompanied by fatigue and pain through the midfoot and forefoot due to increased strain on the tarsal joints, tender callosities may develop under the metatarsal heads.

If one considers only walking with shoes, the ideal position for the fused joint would be such that the axis of weight bearing of the lower limb would make a right angle with a line along the surface of sole and heel of the shoe. This varies with the length of the foot, thickness of sole, and height of the heel. In the average man's shoe the foot is at an angle of 5 degrees. In a size six woman's shoe with a 2½ inch heel and ¼ inch sole it is 20 degrees. Thus maximum dorsiflexion of the foot necessary for a normal gait when wearing shoes may be less in proportion to the height of the heel. This enables those who by misfortune have a persisting equinus of more than 10 degrees to walk normally merely by proportionately increasing the height of the heel.

This does not mean that a woman who has a maximum dorsiflexion of 95 degrees is restricted to a low heel, for if the foot will allow further plantar flexion through the unfused tarsal joints to 110 degrees without strain, as it commonly will, she can have a normal gait wearing a shoe which places the foot in 20 degrees equinus. Therefore, the height of heel that can be worn is governed not by maximum dorsiflexion of the foot but by maximum plantar flexion. However, a barefoot gait is governed by maximum degree of dorsiflexion, which should be 100 to 90 degrees.

Figs 4 and 5 Roentgenograms taken 9 months after fusion of the ankle showing extreme dorsiflexion and plantar flexion of the foot Approximately 45 degrees of anteroposterior motion is obtained through the unfused tarsal joints, most of it taking place through Chopart's joint This patient was 20 years of age at the time of fusion and but little motion had been present in the ankle for several years previous to operation The latter fact probably accounts for the excellent range of compensatory motion in the tarsal joints

This is illustrated by the 2 following cases

CASE 135870 Mrs E R s ankle is arthrodesed so that maximum dorsiflexion of the foot through the tarsal joints is 0 degrees and plantar flexion 115 degrees She has normal gait when wearing a 2½ inch heel, but without shoes has a severe protective limp, weight being borne on the metatarsal heads

CASE 130738 Mrs H H's ankle is arthrodesed so that the foot has a maximum dorsiflexion of 95 degrees and plantar flexion to 150 degrees When walking with or without shoes she is not conscious of any difference in the two extremities nor can one discover any abnormality in her gait

Complete correction of the lateral displacement to a neutral position is desirable Persisting valgus subjects the tarsal joints to abnormal weight thrusts and may cause much generalized foot pain and fatigue Pes varus likewise disturbs the weight bearing relations of the bones of the foot, causes instability and gives the patient a sense of insecurity of gait Full correction of any existing rotary deformity is not so essential but an attempt should be made to place the foot in from 0 to 15 degrees external rotation on the leg Here again the optimum position is neutral If the external rotation is extreme it can be more satisfactorily corrected by an osteotomy through the proximal tibial metaphysis than through the ankle joint.

TECHNIQUE OF ANKLE ARTHRODESIS

The joint is approached by a 5 inch anterior incision in the sagittal plane dividing skin and subcutaneous tissues, and, more deeply transverse crural and cruciate ligaments The extensor hallucis longus and anterior tibial tendons, together with the dorsalis pedis artery vein and deep peroneal nerve, are retracted medially and the extensor digitorum longus laterally The anterior lateral malleolar artery and vein are divided and ligated The periosteum over tibial metaphysis and epiphysis with the capsule of the joint is incised and reflected until the front of the ankle is exposed as far as the malleoli Further exposure of the articular cartilage is obtained by cutting away part of the anterior lip of the tibial epiphysis

The articular cartilage is then entirely removed together with bone sufficient to correct the deformity While any degree of equinus can be corrected by removal of simple bone from the tibia, it is better in severe cases to get rid of as much equinus as possible by lengthening the calcaneal tendon With a curved osteotome opposing surfaces are "fishscaled" so as to make a soft bed of cancellous bone. Using the same incision, bone is gouged from the lower tibial metaphysis and small chips are wedged into the joint, particularly between talus and malleoli This is important because it does away with the space created by removing cartilage and insures firm contact of bone surfaces [1] A few bone chips are placed over the anterior aspect of the joint.

Capsule periosteum, and other deep tissues are reunited with interrupted catgut sutures and the skin with silk

The described method of arthrodesing the ankle must at times be modified to meet unusual situations At some clinics, when the lateral dislocation of the talus is extreme, an incision is made just anterior to the fibula The fibula is divided through its distal metaphysis and sunk in a groove prepared for it in the lateral aspect of the tibia This allows complete reduction of the lateral displacement and decreases the circumference of the leg at the ankle joint

A long leg, plaster-of-paris boot is applied with the knee in slight flexion and the foot in the desired position Six weeks after operation the cast is removed and a short leg walking boot applied The latter is taken off in 6 weeks Physiotherapy is given, walking encouraged, and, if indicated, a steel arch is worn

A STUDY OF ANKLES ARTHRODESED

The first ankle arthrodesis in this series was done January 11 1928 The follow-up period

[1] In individuals who have had extensive poliomyelitis early in their growth period, leaving severely paralyzed leg, the talus largely retains its fetal shape so that the tibial and distal tibial articulating surfaces form arcs of intervital circles In such cases the area of actual bone contact is small and can be increased by the procedure outlined

Fig 6 Anteroposterior and lateral roentgenograms showing varus deformity and osteoarthritis of ankle, secondary to malunited bimalleolar fracture sustained 9 years previously, in a man 45 years of age

Fig 7 Anteroposterior and lateral views of the same ankle as in Figure 6, 5 months after ankle fusion Osseous union present but irregular Clinical result excellent

ranges from 8 months to 5½ years and averages 22 months

Of the 22 patients, 1 was 51 years of age at the time of the operation, 17 between 20 and 50, and 4 were under 20 years They were equally divided as to sex The end-result in the oldest patient of the series, a woman, is excellent

The shortest time after fracture that arthrodesis of the ankle was performed was 1 month, the longest 27 years, and the average 6 years

Nearly all patients were kept routinely 6 weeks in bed wearing a plaster-of-paris cast, followed by 6 weeks up, walking with a short leg cast on the affected extremity All but one had osseous union demonstrated in roentgenograms at the end of 3 months, and in the average case the patient was able to return to his former occupation 4 months after operation

Loss of motion in the ankle joint causes very little disability and is partly compensated by increased motion in the remaining joints of the foot (Figs 4 and 5) Among adults the range of anteroposterior tarsal joint motion following ankle fusion averaged 20 degrees It is still greater in the young About one-half as much motion was present in those who, in addition to the ankle had either a tarsal section or subtalar triple arthrodesis

Most patients had 1 to 1½ inches decrease in the circumference of the leg on the affected side as compared to the normal This much atrophy was often present before operation, however

Two patients had a lengthening of the calcaneal tendon, 2 had calcaneal tendon lengthening plus posterior ankle capsulotomy, 2 had a mediotarsal joint fusion, 1 a subtalar triple arthrodesis, and 1 a talonavicular arthrodesis, in addition to the ankle fusion In the first 6, the additional operations were necessary to get rid of excessive equinus The subtalar triple arthrodesis was done 6 years before the ankle fusion to correct an equino-varus deformity taking place in the ankle-joint itself This partly replaced the foot under the axis of weight bearing but obviously did not restore a normal ankle joint, so that pain and disability continued The talonavicular joint was arthrodesed because the fracture extended into it, and the talocalcaneal joint had undergone spontaneous osseous ankylosis

RESULTS OBTAINED FALL INTO FOUR GROUPS

Group I Excellent A symptomless ankle A gait essentially normal with or without shoes, so that the patient in walking is not conscious of a difference in the two lower extremities This necessitates having the foot in 0 to 10 degrees of equinus, with a good range of tarsal joint motion and neutral lateral alinement or nearly so Eleven of the patients are in this group

Group II Good Ankle or foot symptoms mild or transitory A gait normal with shoes but which may be abnormal without, due to excessive equinus Seven patients fall in this group

Group III Fair One who continues to have symptoms, deformity or excessive equinus yet feels better than before operation, and this subjective sense of improvement is corroborated by the physical findings Two are in this group In one considerable lateral displacement of the talus on the tibia remains and symptoms of foot strain are present In the other excessive equinus has caused aching pain through the anterior portion

of the foot and tender callosities under the metatarsal heads.

Group II Poor Patients not improved or worse than before operation. In this group are 2 men in whom fractures occurred 9 and 16 years, respectively before operation. The fractures entered both ankle and subtalar joints and produced equinus-varus deformities. One had a compound infected fracture originally the other developed infection and a pseudarthrosis following a midtarsal section to correct equinus done 12 years before the ankle fusion. In neither case has the ankle arthrodesis entirely corrected the deformity 20 degrees equinus and slight varus remaining in 1, and 15 degrees equinus in the other In the former the fusion is considered solid clinically but doubtful by roentgenogram Gait and other physical findings reveal slight improvement.

In summary 20, or 91 per cent of the patients are improved by and glad they underwent, the operation Two patients, while not worse are not improved and are therefore dissatisfied

When should the ankle be arthrodesed? Broomhead states There are two procedures alternative to immediate open correction of irreducible fracture dislocations one depends upon the experience of the surgeon, the other upon the function which is a result of treatment by the closed method The first alternative is to wait for about a fortnight until the swelling has been absorbed and then to fuse the ankle joint The second alternative is to allow the patient to obtain the best result possible from conservative means and then, if the function of the ankle in 6 months or so is insufficient for his purpose to fuse the ankle joint As the second of these procedures is based upon the function of the foot rather than the experience of the surgeon, it is surely the sounder one to adopt I mention the first method quite tentatively as I have no experience of it but I suggest that in selected cases much time would be saved if such a course were followed

DEDUCTIONS

In the light of the information gleaned from the 216 patients studied the writer is in accord with Mr Broomhead It is felt that any patient should have the ankle arthrodesed who at the end of 6 months still walks with a limp that is protective or mechanical in origin and in whom roentgenograms of the ankle show failure of complete reduction of the fractured fragments sufficient to account for the physical and subjective findings

As might be expected osteoarthritis is particularly severe and common in incompletely reduced bimalleolar fractures combined with a fracture of the posterior margin of the tibial plafond, and in compression fractures that result in disruption of the weight bearing surfaces of the joint While the policy of waiting for function to decide is the safer the surgeon who has had a great deal of experience in fracture dislocations and arthrodesis of the ankle should not hesitate to fuse selected cases of these types at an early date, thereby saving the patient from several months of discomfort and disability

SUMMARY

1 Of a series of 216 fractures affecting the ankle 88 per cent occurred in adults, and of these 71 per cent were in females

2 Conservative measures gave partial, but seldom complete, relief from symptoms in malunited fractures affecting the ankle

3 The most helpful conservative measure used was wearing a metal arch patterned on a plaster mold of the foot

4 Arthrodesis of the ankle is presented as a satisfactory means of treating malunited fracture dislocations in selected cases

5 The ideal position for an arthrodesed ankle is neutral lateral and rotary position and maximum dorsiflexion such that from 3 to 9 degrees equinus of the foot remains

6 Of 22 patients treated by ankle fusion, 20 are improved by and glad they have had, the operation

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RELATION OF CHRONIC CERVICITIS TO INFECTION OF THE URINARY TRACT[1]

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DURING the past 3½ years, we have had opportunity to study about 400 women patients with urological conditions One year ago Ewert and Herrold reported observations on a consecutive series of 50 patients who were examined for urethral and bladder neck lesions and their relation to the disturbance of urination We found that the treatment of the existing granular urethritis and polypoid excrescences by fulgeration, dilation, and silver nitrate relieved many of these patients of their symptoms With the elapse of a longer follow-up period, we found some of these patients returning with a recurrence of symptoms Clinical observation at that time suggested that in many instances the primary etiological factor was probably due to some gynecological pathology We were further stimulated by the report of Winsbury-White in which he concluded from his experimental work that there was a direct lymphatic connection from the cervix to the urethra and floor of the bladder

Sturmdorf (9) and others have emphasized the importance of the cervix as a chronic focus of infection for systemic disease Moench found streptococci to be the most common bacteria present in chronic cervicitis This was confirmed by Maryan, who found streptococci in a high percentage of infections Also, he found by further laboratory tests that these streptococci were of the group known as enterococci, which are difficult to isolate on primary cultures, and whose outstanding characteristic is their ability to resist heat to 60 degrees C for a longer time than other streptococci

This series of 32 patients had some or all of a group of symptoms, the outstanding of which were frequency of urination with burning, intermittent deep pain above the pubis which was evidently at the neck of the bladder, low backache, and less frequently, radiating pains into the groin, the thigh, and upward along the course of the ureter Many of these patients had pronounced leucorrhea

This syndrome is frequently described as irritable bladder Epstein and Ovtschinnikov published an article in 1931 on the pathogenesis of cystalgia in women when the urine is free from bacteria They believe that infection is not an essential etiological factor, but rather is due to repeated circulatory disturbances in the small pelvis from menstruation, coitus, pregnancy, etc They state that without a doubt a lasting vascular engorgement can produce chronic inflammation without the help of infection It was our observation that bacteria may be found in every urine of patients with irritable bladder by making careful smears and cultures of the urinary sediment, although in many instances the smears do not reveal more than an occasional pus cell Epithelial cells are more constant Culture results in the latter part of this series yielded streptococci in a large percentage of the non-colon bacillus infections when an improved medium was used

Twenty-nine of this series of 32 patients were followed for a sufficiently long period to permit of analysis Coagulation of the cervix was done in each instance A second or third coagulation was done on a few of the patients The results as measured by relief of symptoms relative to the urinary tract are divided into two classes The first included those in whom no improvement or but slight improvement followed coagulation of the cervix There were 5 patients who had no improvement, and 5 who had but slight improvement The second class included those who reported marked improvement of whom there were 11, or complete relief of whom there were 8 Therefore, it may be noted that 19 of 29 patients, or approximately two-thirds, had a satisfactory clinical response as to their urological symptoms following coagulation of the cervix In the total series, there were 12 patients in whom the cultures revealed colon bacilluria alone or associated with other organisms, while 17 had predominant bacterial flora of mostly coccal types, usually streptococci Further analysis indicated that 7 of the 10 non-responsive patients were those with colon bacilluria, while 14 of 19 who had satisfactory relief of symptoms were non-colon bacilluria infections This would seem to lend support to the view that the secondary focus in the urethra and bladder is the result of continual inoculation by way of the lymphatics from the cervix, since it is well known that metastasis is much more likely to occur by streptococci as compared to colon bacilli

In approximately two-thirds of this series cultures were also made of the cervix to compare the

[1] Read before The North Central Branch American Urological Association Cleveland, November 8, 1934

growth with that from the urine sediments In many instances like-streptococci were isolated from cultures of both areas These streptococci are very difficult to grow on artificial medium giving small pin point colonies. While we have not made an absolute identification of the species, it seems certain that they are a member of the enterococcus group They do not produce hemolysis or greening of the blood agar when first isolated and would be termed indifferent streptococci as regards their reaction on blood agar Direct smears as a rule reveal pleomorphic forms, often more gram negative than gram positive Cultures were made of the cervix of 10 colon bacilluria patients Seven yielded no colon bacilli from the cervix, a but two or three colonies, and in 1 instance only, there was a predominant growth of colon bacilli. This observation would seem to indicate that like flora of the cervix and urine, sediment was not dependent at the time of culture on recent inoculation of each other by way of the vagina or urethra

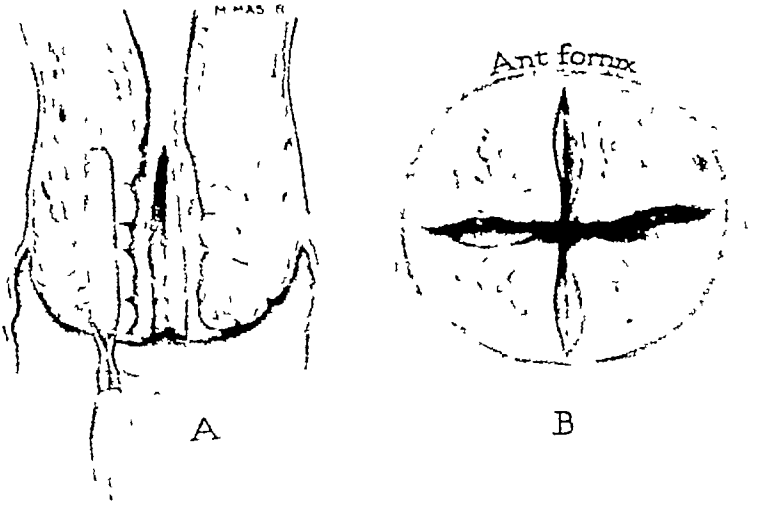
CHRONIC CERVICITIS

The base of the bladder is intimately connected below to the anterior surface of the supravaginal portion of the cervix and above as far as the area of the internal os. This area is the anterior part of the base of the broad ligament or parametrium which is known as the cardinal ligament of the uterus, and is its main support In this area, between the peritoneum and the pelvic fascia, is incorporated the uteropubic ligament, an abundance of loose areolar connective tissue smooth muscle fibers a rich network of lymphatics, and blood supply This is the weak spot that is stretched or ruptured during parturition and later contributes to the development of cystocele Normally its depth measures about one-third of an inch It is logical to assume that such intimate histo-anatomical relationship would enable chronic cervicitis to be a factor in the production of an irritable bladder either by direct extension or most likely through the lymphatics This histo-anatomical lymphatic relationship is not brought out in the various textbooks dealing with the anatomy and lymphatics of the bladder and cervix of the uterus Winsbury White has fully demonstrated, experimentally by injection of India ink as well as living and dead tubercle bacilli into the cervices of guinea pigs and rabbits that not only is there lymphatic connection between the bladder and the cervix, but also between the cervix and vagina In chronic cervicitis there is also a perivascular lymphocytic infiltration, and a paracervical parametritis

It is accepted among gynecologists that chronic cervicitis is due to a persistent infection in the depths of the compound racemose glands, which is characterized pathologically by a perglandular round cell infiltration The cervix is prone to infection because of its situation in the vagina and because it is lacerated during labor The crypts and lacunæ of the mucous membrane afford a protection for the invading organisms, and in these areas the gonococci and other bacteria may lie dormant for long periods of time

Investigators agree on the bacterial flora of the surface of the pathological cervical canal, but no mention has been made of the bacterial flora in the depths of the glands Marvan, after grinding under aseptic technique the cervical tissue which was enucleated equally by Sturmdorf's (10) method and coniation with the high frequency cutting current scalpel, isolated the heat resistant enterococcus from the depths of the compound racemose glands in 80 4 per cent of the patients He has shown bacteriologically and pathologically that chronic cervicitis is a deep infection of the compound racemose glands, which is characterized by a perglandular round cell infiltration, and by a perivascular lymphatic lymphocytic infiltration of the deep connective tissue stroma or musculature Therefore it can be seen that the glandular structure of the compound racemose glands encountered in the stratified squamous epithelium of the portio-vaginalis portion of the cervix (the vaginal portion of the cervix which is normally free from glands) is due to an extension of the proliferation of the normally present compound endocervical racemose glands This extension of the proliferation is referred to in the literature as an erosion, a term which of course is a misnomer as it is not a substitution of the stratified squamous epithelium by the cylindrical epithelium of the endocervix primarily but a downward displacement of the compound racemose glands, with its associated inflammation and regeneration Rightfully it should be called chronic pan cervicitis or chronic cervicitis, as the entire cervix is invaded Therefore with this understanding of the pathological genesis of chronic cervicitis, one is enabled to treat cervical lesions adequately Macroscopically erosion or chronic cervicitis is evidenced by redness of varying degrees of the cervical lips surrounding the patulous external os, together with an abundance of mucopurulent secretion from the cervical canal It has been customary to classify these changes under the following clinical divisions

1 Congenital erosion—This lesion is encountered in virgins or young girls



Spatula tip *in situ* indicating that contact is made against the edge of the blade
Figure at right shows the depth of the linear striping of the cervical canal

2 Ectropion or eversion of the cervical lips, which is truly not an erosion but a velvety red bulging forward of the endocervical mucous membrane breaking through the mucocutaneous junction, normally situated inside the external os

3 Simple erosion, which is a replacement of the stratified squamous epithelium of the cervical lips by the high cylindrical epithelium

4 Follicular erosion, which is characterized by the presence of retention cysts, the so called Nabothian follicles or cysts

5 Papillary erosion, and it is manifested grossly by velvety red elevations on the surface of the cervical lips

6 The healing of erosions, or replacement of the glandular misplaced epithelium with stratified squamous epithelium

These terms may be conveniently retained as long as we bear in mind that they represent only progressive grades in the same pathological process of chronic cervicitis

TECHNIQUE OF COAGULATION

The heavy mucoid discharge from the cervix is dissolved and removed with caroid powder, which dries the canal and makes its surface more visible No local anesthesia is used in the cervix A tenaculum is not used to hold the cervix in place for the reason that adequate exposure may be obtained with Guttman's operative speculum Coagulation is done preferably between the fifth and the fifteenth day after menstruation since complications are less likely to follow if carried out at this time

Other lesions of the cervix should be ruled out before coagulation, such as syphilis, tuberculosis, early carcinoma and pin point leucoplacias Because of the rich supply of lymphatics capable of producing such associated lesions as metritis, parametritis, and uterosacral cellulitis, it is advisable also to rule out any chronic inflammatory residual pelvic pathology Coagulation of the cervix should never be done in the presence of an acute or subacute inflammatory lesion of the internal or external generative organs

The short circuit method of diathermy coagulation was used with the indifferent tin plate electrode under the patient The spatula tip (3 centimeters long by 3 millimeters wide) positive electrode (Fig 1), was used for coagulation of the cervix The proper dosage with the universal Bovie machine is obtained by setting the indicator on 40 of the coagulation meter scale which gives the proper milliamperage

Where the cervix has an edematous and acutely inflamed appearance associated with marked lacerations, it is best to treat it first by topical applications of 10 per cent tannic acid and glycerin into the cervical canal, supplemented by daily hot douches This will shrink the cervix materially and reduce the activity of the chronic inflammatory process

We have employed routinely the linear striping of the cervix commencing within the internal os extending to the external os and continuing this linear striping on the cervical lips, at right angles to the linear striping of the cervical canal (Fig 1) The edge of the spatula tip electrode was found most suitable The tip is first placed firmly against the cervical tissue and then coagulation is begun. The coagulation of the cervix was usually completed in one sitting The amount of coagulation should be sufficient to reach beyond the gland bearing tissue and into the adjacent stroma. In this way sufficient destruction of the infected gland bearing tissue will be produced, as well as adequate drainage

Usually the crucial incisions were made at 12 3 6, and 9 o clock for hypertrophic eroded cervices with bilateral lacerations In some instances with marked hypertrophy of the upper lip additional linear striping was done at 11 and 1 o clock However one must individualize the extent of coagulation in different patients The failures that occur following coagulation or cervical plastics are usually due as shown microscopically by Koster and by Wolfe, to remnants of the uppermost infected gland bearing tissue near the internal os Further coagulation, if necessary is done after 3 weeks, since the height of the tissue reaction has subsided by this time Fractional coagulation is preferable for chronic gonorrheal infections and in general office practice

A few patients complain of mild to severe cramp-like menstrual pains during coagulation, but as a rule they are transitory Patients are instructed to abstain from the use of douches during the postcoagulation period Close postoperative observation is given with cleansing of the wound as indicated Epithelization is usually complete between the fourth and sixth weeks

Three possible complications may follow coagulation of the cervix, namely hemorrhage stenosis, and pelvic infection Bleeding during the days immediately following cervical coagulation is usually benign and due to the oozing of the sloughing surface Very infrequently severe secondary hemorrhage is encountered about the twelfth to the fourteenth day as a result of too extensive coagulation There will be a slough beyond the area of coagulation because of the deep penetration of the generated heat On this account severe secondary hemorrhage may occur from sloughing of the cervical branch of the uterine artery in the region of the internal os where coagulation has been too extensive Stenosis is avoided by follow-up dilatation of the cervical canal as employed by Curtis

RECAPITULATION

While this work was in progress a personal communication was received from Dr J Howard Shane regarding unpublished work which he has done in co-operation with a gynecologist, Dr Mabon Their results parallel ours very closely as regards clinical proof that adequate treatment of chronic cervicitis is followed by relief of many of the so called "irritable bladders." They believe that cauterization of the cervix does not give the greatest benefit unless follow-up treatments are given for several weeks. Their postcauterization management consists of dilatation of the cervical canal, and application of silver nitrate to the cervix, both internally and externally at intervals of one week. Certainly as we have emphasized, dilatation of the cervical canal is an important follow-up measure

As mentioned, our clinical results indicate that treatment of the cervix as described gives satisfactory relief of symptoms referable to the urinary tract in approximately two-thirds of the patients As yet our investigation has not proved the exact mechanics of such improvement We lean to the view that constant reinfection of the urethra and bladder particularly with enterococci is an important contributing factor In many instances, clinical improvement has been coincident with a decrease of the bacterial flora of the urinary tract On the other hand some patients with improvement have continued to yield enterococci from cultures of the urinary sediment It is possible that such remaining infection is more superficial than before cervical coagulation, and would disappear spontaneously or by treatment after a longer period had elapsed Further investigation is required before the exact mechanics of improvement can be established

It has been emphasized by others that the cervix frequently is a focus of systemic infection particularly arthritis and iritis One arthritic patient in our series was relieved of all symptoms within 4 weeks after coagulation of the cervix

There were 2 patients in our series who had symptoms similar to a group that is frequently described as idiopathic fever Kastner and Rowntree in an analysis of 100 cases of long continued low grade idiopathic fever state that females constitute almost three fourths of their entire group A diagnosis of tuberculosis had been made in both of these patients and one had been sent to a sanatorium in New Mexico where, after several weeks of observation it was decided that she was not tuberculous After coagulation of the cervix in this patient the temperature returned to normal and the urine cultures no longer yielded

streptococci The second patient continued to have fever after coagulation but streptococci persisted in the urine cultures and it is possible that all of the infected gland bearing tissue was not destroyed In such instances the Sturmdorf operation would seem preferable

It is well known that the incidence of interstitial cystitis is higher in women than in men One patient of our series with an early interstitial cystitis had definite improvement following coagulation of the cervix A further study is being made to determine a more exact relationship between infection of the cervix and this type of cystitis

SUMMARY

In a series of 32 patients with irritable bladder, there was complete relief or marked improvement in two-thirds of the series following coagulation of the cervix

Improvement occurred more frequently in patients with streptococcus infection as compared to those with colon bacilluria Most of these patients had macroscopically clear urines and the sediment revealed bacteria with but few or no pus cells The heat resistant so called enterococcus group was the most common type of streptococcus isolated in the examination and study of the urine sediments

The infected gland bearing tissue of the cervix was destroyed by deep crucial incisions It is necessary that coagulation be followed by dilatation of the cervical canal including the internal os

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Fig. 1 Fig. 3 Fig. 5

Fig. 1 First recurrence, a scar, right side. Reduced 1/6
Fig. 3 Metastatic nodule, left breast. Reduced 1/6
Fig. 5 Tumor, left axilla, skin, nodes, 2. Reduced 1/6

Fig. 2 Scirrhous carcinoma, peripheral area of first recurrence (Figure 1). × 70

Fig. 4 Nodule of scirrhous carcinoma, metastatic in left nipple (cf. Figure 3). × 70

Fig. 6 Lymph node, left axilla, with malignant invasion (Fig. 5). × 70

Fig. 7 Skin of left axilla (irradiated) with Paget like changes and malignant [illegible] (cf. Fig. 5). × 70

CARCINOMA OF THE BREAST

Survival for 24 Years with Local Recurrences and Metastases in the Opposite Breast and Axilla

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From the Laboratory of the Royal College of Physicians Edinburgh

ALTHOUGH the survival for many years of patients who have been subjected to radical operation for carcinoma of the breast is comparatively common, the successful treatment of a metastatic growth in the opposite breast and secondary invasion of lymph nodes in the opposite axilla appears to be sufficiently rare to warrant the publication of the case

In 1910 the patient, a married female aged 47 years, primipara was admitted to the Edinburgh Hospital for Women and Children, where Dr Elsie Inglis performed a radical operation for scirrhous carcinoma of the right breast. The pectoral muscles were removed and the axilla cleared

In 1921, the patient aged 58 years, was re admitted to undergo an operation for uterine prolapse The menopause had been complete since the age of 50 and her health had been excellent. On examination, the operation scar was noted to be sound and healthy except for a small scab at the lower end which had persisted since the operation

In 1922, she reported with a small lump at the lower end of the scar noticed 10 days previously and increasing in size with redness of the skin Examination showed a hard lump the size of a florin, disc shaped and lying in the thin tissue over the fifth intercostal space It was movable on the chest wall, but the overlying skin was fixed, red and glazed One and one half inches lateral to it was a second nodule the size of a pea

At operation both nodules were removed with a sufficient ellipse of skin and subcutaneous fat Histological examination revealed that the nodules showed scirrhous carcinoma with tumor cells present near the skin margins (Fig 1, the larger nodule, and Fig 2)

In 1931, the patient reported with a swelling in the left (opposite) axilla, present for 12 months and gradually increasing in size, with occasional ulceration and the discharge of an offensive yellow fluid Examination showed a small mass in the left axilla which appeared to consist of several lymph nodes matted together, about the size of a golf ball and adherent to the underlying tissues The skin overlying was inflamed and fixed, and serous fluid exuded on pressure At the same time, the scar on the right side showed three separate, flat, reddish nodules fixed to the underlying tissues about the midclavicular line No clinical lesion was found at this time in the left breast The left axilla was treated by one of us (M C T) with 100 milligrams of radium at 2 centimeters and the three nodules in the original scar with 25 milligrams at 1 centimeter on surface applicators, each application delivering one skin erythema dose (600,000 ergs per cubic centimeter)

Three months later there was still a tumor the size of a walnut in the left axilla, it was scabbed and still fixed to the skin but was now movable over the deeper tissues. The left nipple now showed a slightly reddened area on its lateral aspect and was scaly, on palpation, the discolored area felt thickened The thickened area in the left breast was excised locally, with the nipple (Figs 3 and 4) The nodes in the left axilla with the surrounding fat and the overlying skin were dissected away (Figs 5–7)

Since this last treatment early in 1931, the patient has remained under supervision and has been very well She was employed as a cook in an Institution since the first operation in 1910 until 1933, when she regretfully retired on her old age pension

She was examined and photographed in September 1934 (Fig 8) At the age of 71, she feels well and able to do her own housework and to help to nurse an invalid The scar of the primary operation (right side) shows an area of very dark pigmentation with some hyperkeratosis but no sign of active disease. The left breast shows a linear scar in place of the nipple but is soft, movable, and appears normal for a woman of this age There is a scar in the left axilla but it is perfectly movable and there are no palpable nodes. No nodes are palpable in either supraclavicular region There is no cough no shortness of breath no swelling of the abdomen Sometimes she feels a little stiff but has no pain anywhere

Fig 8 The patient in September, 1934, aged 71 years, 24 years after primary radical operation (the darkened area in the scar is largely pigmentation)

[1] Carnegie Research Fellow

Histology of the different areas examined The original operation tissue is not available The first recurrence in the scar shows glandular carcinoma, a typical scirrhous growth (Fig 2) The nodule from the left breast shows a similar histological structure (Fig 4) though somewhat more cellular In our opinion, the position of the nodule (Fig 3) the nature of the growth, and the absence of involvement of the mammary gland tissue suggests metastatic tumor rather than a new and independent neoplasm in this opposite breast The axillary tissue on this side shows malignant infiltration reaching to the skin and two small nodes invaded by cancer cells (Figs. 5, at x 6, and 7) The cells are active in spite of irradiation The Paget like changes in the axillary skin and the small cystic areas with partially necrotic tumor cells may be due to radiation treatment (Fig 7) This left axillary area of carcinoma may be an independent metastasis but, more probably, is a secondary spread from the skin nodule in the left nipple, though the latter became evident clinically at a later stage

It is not suggested that there is any special interest in the method of treatment, which merely followed the manifestations of the disease. The unusual feature is the extraordinary degree of resistance shown by this patient to the malignant growth. The survival is not exceptional. At the Clinical Congress of the American College of Surgeons in 1932 where special emphasis was laid on the curability of cancer Wainwright reported 3 cases well and apparently cancer free for over 20 years, though none showed recurrence or metastasis Guthrie reported 1 case well for 16 years and McLean 9 cases well for 15 to 25 years Pfahler and Parry[1] reported 22 cases alive 20 to 22 years after treatment 6 of these had recurrences treated, none had metastases. Our patient had malignant tumors of the opposite breast and axilla which, from the clinical course and result of treatment, we consider are probably metastatic, a primary growth in the second breast and axilla is unlikely to have remained clinically cured for nearly 4 years after local excision of superficial nodules The mode of involvement of the second breast is obscure in the absence of any clinical evidence of spread across the sternum.

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SYPHILIS OF THE BLADDER

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IN reviewing the literature on syphilis of the bladder, one is struck with the laxity with which cases are reported The controversies regarding its rarity depend entirely upon the criteria used in diagnosis, and not upon the power of observation or diagnostic acumen of the contributors As yet, not one case reported has measured up to the standard set by Young, who maintains that the diagnosis cannot be categorically proved unless the treponemata be demonstrated in the lesions

INCIDENCE

The incidence varies strikingly with the observer Chocholka (2), who seems to be the most prolific contributor, added 6 more cases in 1931 to 56 others he had seen since 1911 In 1923 (3) he reported 14 cases from his own practice, 18 cases collected from a series of 105 cystoscopies at the clinic at Prague, and 13 observations of parasyphilis, and in 1928 (4) he added 11 new cases, making a total of 56 cases Chocholka stated that in 1900 the literature contained only 14 cases, whereas in 1925 he was able to collect 169 cases The writer has collected a series of 158 cases which have been analyzed The discrepancy between this number and that of Chocholka arises from the fact that no cases are included prior to 1900 Thirty-nine cases of Chocholka (5) reported in 1926 and 30 cases of Duvergey are not included nor are the several cases in unobtainable foreign periodicals Valverde (1932) reports that of 201 patients complaining of vesical symptoms, upon whom 282 cystoscopies were performed, 57 were diagnosed and treated as vesical syphilis Raunch (1930), in a series of 53 routine cystoscopies upon cases of lues, found 4 with evident bladder manifestations which were diagnosed as vesical syphilis Young is very skeptical about the cases reported, not having seen any himself, and Levy and Zimmerman, who undertook to determine the incidence, found no lesions in 25 cases of secondary syphilis examined cystoscopically The rarity of syphilis of the bladder is attested by such pathologists as Kaufman, Aschoff, and MacCollum, who either do not mention it or refer to it through the medium of cases reported in literature Evidently, none of these pathologists has personally seen a case or examined a specimen Stokes states that "between 1916 and 1924 no undoubted case was observed at the Mayo Clinic" In the past 25 years neither Dr Beer nor any of his assistants on the Urological Service at the Mt Sinai Hospital has observed a case of syphilis of the bladder

There is no reason to believe that syphilis of the bladder does not exist The spirochæta has invaded every tissue of the human body, but its demonstration has been rendered especially difficult in epithelium lined structures as the lung, stomach, and bladder

PATHOLOGY

In spite of the number of cases reported, only a few observers have investigated the histopathology Denslow (1918) is credited as being the first to make a diagnosis of syphilis of the bladder on the basis of the histopathology On suprapubic cystotomy, he curetted lesions which were examined and reported to him as syphilitic condyloma Unfortunately, he does not give a detailed description of the histopathology in his case report The case reported by Danforth and Corbus was also operated upon and the pathology reported by Dennie as follows "The lesion is seen to consist of two parts—an upper dense, finely striated portion about 4 millimeters thick and a lower narrow core Microscopically, the former shows many slender epithelial fingers connected above by thin bridges and below penetrating the corium" Although Pugh reports that he found typical syphilitic histopathology in the tissue of one case and a suggestive histology in another, a detailed description is not available Valverde describes the histopathology on his first case as follows "Hyperplasia of endothelial cells with slight infiltration of mononuclear cells of chronic inflammation, lymphocytes, and plasma cells Cystic cavity in center with degenerating cells One part was homogeneous (without structure) showing necrosis The second case showed chronic inflammation with hyperplasia of the epithelial lining, one section showing a tendency to anaplasia In the chorion there was an infiltration of the cells of chronic inflammation"

Only eight contributors (Graff, Denslow, Saelhof, DeGouvea, Danforth and Corbus, Pugh, Valverde, and Levy and Tripoli) have subjected the lesions to microscopic study Only the case of Levy and Tripoli presents typical syphilitic

histopathology the photomicrographs showing endarteritis with thrombosis, perivascular lymphocytic infiltration, occasional multinucleated giant cells and small areas of necrosis. The specimens were removed from the bladder at autopsy but the photomicrographs do not show the relation of the syphilitic changes to bladder mucosa Furthermore, the bladder was entered accidently during the operation and a fistula resulted from the attempt to dissect the gummatous mass from the outer wall of the bladder Of the other cases reported in detail, not one presents a specific pathological picture which could be diagnosed as syphilis However it has been argued that the lesions closely resemble those of condyloma lata. McCarthy describes the histopathology of condyloma lata as follows "The epithelium undergoes gigantic acanthosis, the superpapillary portion is greatly hypertrophied and the interpapillary rete cones are enormously elongated and drawn out. The latter often grow in an irregular fashion producing lateral branching or daughter" processes The whole epithelium is saturated with edema to a marked degree and the cells appear larger than normal, due to this absorption of fluid This type of lesion offers a beautiful example of intracellular and intercellular edema For the most part the cells stain badly or not at all. The intercellular spaces are dilated, and wandering leucocytes can be seen making their way through the epithelium In well developed lesions these cells unite to form small collections, causing dissolution of cellular structure and thus producing small abscesses. The infiltrate has a uniform density in the papillary bodies, while it forms a thick mantle about the vessels of the subpapillary and lower layers of the cutis"

This description corresponds rather closely with the histopathology of the cases reported by Danforth and Cobus, Valverde, and the case reported by myself although the last is certainly not a proved case. It is argued that if there is nothing specifically characteristic in the pathology of condyloma lata, there is no reason to expect that the pathology of bladder syphilis should be characteristic. The combination of a mucous surface irritation and syphilis is known to produce the lesions characteristic of syphilitic condyloma which are commonly found about the anus There is no difficulty in establishing their identity since they are teeming with treponemas, but this difficulty has not yet been surmounted in the case of bladder syphilis Here, the same combination of factors exists and the lesions are, therefore, presumed to resemble condyloma lata histologically

SIGNS AND SYMPTOMS

Grossly a variety of lesions have been described on cystoscopic observation. These seem to depend upon the stage of syphilis and the duration of the illness. Although some writers claim that the lesions are sufficiently characteristic to make a diagnosis others state that they resemble the lesions of tuberculosis, malignancy papillomata and bilharziasis. Although some of the lesions, especially the villous vegetating growths and the papules appear to present a typical cystoscopic picture the writer will not attempt to go into the description of the various lesions seen, since he does not believe that these help in the diagnosis

The symptoms are those of any vesical irritation, namely frequency dysuria, tenesmus, depending upon the reduction in the bladder capacity and at times hematuria

Cystoscopically the lesions reported have varied from the appearance of a simple cystitis to the most extreme pictures of tumor with ulceration Most frequently the lesions are situated on the trigone about the ureteral orifices and sphincter

DIAGNOSIS

The case that would receive preference in the diagnosis would present the following factors (1) A previous history suggesting syphilis (2) the presence of active syphilis in the form of a generalized rash, mucous membrane lesions, adenopathy gummata, or ulcers elsewhere (3) a positive Wassermann (4) the absence of all other etiological factors (5) a rapid amelioration of the symptoms with disappearance of the lesions as shown by cystoscopic control following the institution of antiluetic treatment.

The chief discussion of all cases of bladder syphilis revolves about the criteria used in making the diagnosis If any one of the factors mentioned be taken by itself it could be easily eliminated as substantial proof of the diagnosis We must revert to the finding of the spirochaeta as the only method for categorically proving any case In view of the fact that the spirochaeta has never been found either in the lesions or in the sedimented urine, we must discard all the cases reported or select a few which offer the maximum of corroborative clinical findings

Assuming that a hypothetical case presents the signs of activity a positive blood Wassermann, and responds rapidly to treatment, we cannot very well discard it in spite of the absence of spirochaetæ or distinctive pathology It has been shown that stomach syphilis presents no uniform or distinct syphilitic pathology It is hoped that

further study will decide the actual histopathology of syphilis of the bladder by concomitant finding of the spirochæta

Then, only, may the non-specificity of the histopathology be established and eliminated as one of the required factors

Chocholka and Valverde have entered into a controversy over the relative merits of the cystoscopic appearance and the response to treatment as guides to diagnosis Obviously, the latter is the more important However, we know that the arsenicals and mercury especially when given intravenously, are excellent remedies for ordinary coccal or bacillary infections of the genito-urinary tract The manner in which neoarsphenamine produces a cure is not well understood Friedman showed that it decomposes into formaldehyde, but he rated this quantity as only 000004 per cent If this amount were effective, cures should be expected with much larger doses of urotropin, which has been ineffective in ordinary coccal infections and in cases reported as syphilis of the bladder

The strength of the argument for the therapeutic test has been increased by the results obtained by the use of bismuth alone in the antiluetic treatment

PROGNOSIS

If a case is established as one of syphilis of the bladder by the therapeutic test, it follows that the prognosis must be uniformly good Most of the observers have based their case reports upon the rapid response to treatment which has been striking A few cases of recurrence of symptoms and lesions have been reported Correa cites 3 cases observed between 1923 and 1929 Each one was originally diagnosed as syphilis of the bladder by cystoscopic findings and the response to treatment When they recurred, they again responded to antiluetic treatment. In the series of 158 cases reported here, 5 cases showed evidence of recurrence Only 1 was definitely cured, 2 were reported still under treatment, 1 died, and the other was not controlled

CASE 1 B L, married, female, aged 55 years, gave a history of having been treated for a gonorrheal infection about 1 year prior to her admission to the X Hospital While she was treated for the gonorrheal infection she had no urinary symptoms Beginning about January, 1928, she began to have marked frequency of urination, dysuria, and incontinence She was admitted to the X Hospital on February 21, 1928, and discharged March 9, 1928 Cystoscopy showed a marked congestion of the entire bladder wall, more marked around the trigone with necrotic areas in that region There was marked bullous edema The ureteral orifices were normal The sphincter margins were markedly congested X-ray examination of the genito-urinary tract showed a small calcific shadow

Fig 1 Cystogram of Case 1 (B L) taken May 25, 1928, at the time the patient was suffering intense dysuria and tenesmus The great diminution in bladder capacity and the expulsive effort are responsible for the reduplication and the small size On the left lateral wall is seen the filling defect corresponding to the vegetating growth observed cystoscopically

the size of a split pea at approximately the left ureterovesical orifice The kidneys were normal in size, shape, and position The urine contained many pus cells in clumps The blood chemistry showed non protein nitrogen, 30 milligrams, urea, 14 milligrams, uric acid, 2 3 milligrams, and sugar, 91 0 milligrams The blood Wassermann was negative. The blood pressure was 175/85 The blood count showed red blood cells 3,900,000, hemoglobin, 70 per cent, white blood cells, 9,400, with 72 per cent polynuclears and 28 per cent lymphocytes She was discharged from the hospital with a diagnosis of hypertension and chronic cystitis

She was admitted to Y Hospital on May 5, 1928 The complaints were the same as on admission to X Hospital. She was found not to be acutely ill The right pupil was greater than the left and reacted sluggishly to light. The skin showed a maculopapular rash involving the face, trunk, and extremities This was diagnosed as a papular eczema on May 7 by the dermatologists, but on May 9, 1928, the blood Wassermann was reported 4+ and on May 14 the diagnosis of the skin condition was changed to a secondary syphilide On May 7, the urine showed specific gravity of 1010, acid reaction, trace of albumin, some epithelial and white blood cells

On the same day, urea nitrogen was 21 8 milligrams and sugar 112 milligrams On May 10, 1928, mixed treatment consisting of 1 dram of the mercury and iodide mixture was administered three times daily Bladder irrigations with 1 5000 acriflavine were given twice daily beginning on May 15 and 15 minims of tincture of hyoscyamus was given three times a day beginning May 10 In spite of this treatment, the patient still presented the same symptoms with intense dysuria and frequency so that she voided every half hour during the day and four or five times during the night. On May 22, 1928, she was subjected to a cystoscopic examination by the writer and a marked diminution in bladder capacity was noted The region of the left ureter, the left lateral wall of the bladder and the trigone on the left side, extending down to the sphincter, was a site of a vegetating growth The lesions were villus-like, yellowish pink, translucent, and sprang

Fig. 1. Cystoscopic appearance of "vegetating syphiloma" described by Corbus and Danforth (Case 32 in chart) believed by many observers to be typical of bladder syphilis.

directly from the floor of the bladder. There was no pedicle or frond like appearance. There was bullous edema toward the sphincter. The right ureter orifice was normal and the left ureter orifice could not be seen because of the vegetating growth. Bladder urine was cultured and showed only a few colonies of Staphylococcus albus and the guinea pig inoculated with bladder urine showed no evidence of tuberculosis. Smears of the centrifuged sediment revealed no tubercle bacilli.

A cystogram made on May 28, 1928, showed the great reduction in the bladder capacity which was evidenced by the patient's symptoms. The patient was unable to retain more than 1 to 2 ounces of the opaque material, so that an adequate visualization could not be obtained. But the left lateral wall of the contracted bladder revealed an irregularity which corresponded to the distribution of the lesion seen through the cystoscope. The patient was given antiluetic treatment in the form of neosalvarsan 0.45 grams on May 9, May 23, and June 5, and an injection of bismuth on May 29.

The original blood Wassermann, which was 4+ on May 9, became negative on May 28 and again 4+ on June 4, 1928. Under antiluetic treatment there was a marked and rapid amelioration of the bladder symptoms so that on May 24 there was only very slight dysuria and the patient was voiding every hour or two throughout the day instead of every half hour and only three times at night. On May 24, the skin rash had faded considerably.

On May 26, 1928, a second cystoscopy was performed by the writer and specimens were removed from the illcers masses by means of an operating forceps. Unfortunately Levaditi stain could not be made because the specimens were immediately placed in formalin. The histopathology showed a marked proliferation of the epithelial lining with projections above the level of the bladder mucosa and gland like inclusions of epithelial elements. There was moderate edema with round cell infiltration. There was no typical endarteritis, perivascular infiltration, or areas of focal necrosis. The interpretation by Dr. Paul Klemperer was "cystitis glandularis."

Following the patient's discharge from the hospital, antibiotic treatment was continued by means of the injections of neosalvarsan 0.45 grams twice weekly so that she had had eight injections up to July 25, 1928, and two injections of mercury salicylate and five of oxycyanide of mercury. On this date, there was a marked improvement in her general condition. She looked well, had gained weight, and there was no skin rash. There was no frequency or urgency and no burning on urination. She voided only three or four times during the day and twice at night. The urine was entirely clear. Cystoscopy on July 25, 1928, showed several small, irregular elevations about the left ureter orifice. These excrescences were much smaller than those seen on primary cystoscopy and were localized above the left ureter orifice only. The trigone and right ureter orifice were normal in appearance. The bladder capacity was normal.

Specimens were again removed for biopsy and these were reported as showing also a cystitis glandularis but the later specimens showed more edema and round cell infiltration and foci of large swollen endothelial cells (foam cells) and foci of necrosis.

The patient was again seen on December 6, 1928, at which time she made absolutely no complaints. There were no bladder symptoms and she was still receiving neosalvarsan and mercury every week with the exception of one month rest. The blood Wassermann taken about November 1 was 2+.

On April 3, 1929, there were absolutely no urinary symptoms and the urine was crystal clear. Cystoscopy revealed the bladder to be entirely normal. Cystogram made on this date showed a perfectly normal bladder with normal capacity.

Up to this point, a review of the case would leave one with the impression that he were dealing with a well established case of syphilis of the bladder. Had the case been reported in 1929 and not followed until the end of 1931 this error would undoubtedly have been made.

The patient was not seen again until the spring of 193 when she again complained of frequency, dysuria, and tenesmus. She was not examined but referred to the Mt. Sinai Hospital for further study. However, she was not admitted immediately and thereupon made the rounds of several hospitals where diagnoses of chronic cystitis and malignancy of the bladder were made.

She entered the Mt. Sinai Hospital on August 30, 1931, on the service of Dr. Edwin Beer and was discharged on November 17, 193 with the following diagnoses: left renal tuberculosis, arteriosclerosis with psychosis and cerebral changes and lues (?). A summary of her stay is as follows: Complaints of frequency, dysuria, and hematuria for 6 months. X-ray films of the genito-urinary tract on August 31, 1931, revealed normal right kidney, left kidney not visualized, numerous calcific shadows over both kidneys.

Roentgenograms of the chest on August 3, 193 revealed nothing except some cardiac hypertrophy. Cystogram on September 2, 1931, was normal. Electrocardiogram on September 1931, showed left ventricular preponderance. Cystoscopy on September 193 by Dr. Beer revealed bladder urine to be turbid, right indigo carmine excretion was strong. Left ureter orifice was retracted, normal lip converted into an extensive polypoid mass, the orifice being congested and patulous. Right ureter easily catheterized. Left ureter obstructed at 12

Specimens	Bladder	Right	Left
Indigocarmine		Strong	Poor
Microscopic		Negative	Loaded with white blood cells
Sediment for tuberculosis	Negative	Negative	Negative

Fig. 3 Cystogram of Case 1 (B I) taken April 13, 1929 showing the normal bladder capacity and the restoration of normal contour 1 year after the patient had received antiluetic treatment

centimeters 20 cubic centimeters of purulent urine aspirated

Tissue punched from the polypoid mass reported as acute inflammation, no evidence of tuberculosis Guinea pig inoculations of both the right and left specimens were negative for tuberculosis

However, Dr Beer felt he had enough evidence to warrant an open operation, and on September 4, 1931, a left nephrectomy was performed The specimen was reported to show tuberculosis of the left kidney with atrophy and tuberculosis of the ureter

Later, the bladder urine taken on September 3, 1931, gave a positive result for tuberculosis, on animal inoculation Cultures from both kidneys were negative On September 1, 1931, Wassermann was negative and spinal tap was not made Following the operation, an extensive wound infection developed which required dakinization and healed with great difficulty Specimens punched from the wound failed to reveal any tuberculosis, either histologically or on guinea pig inoculation

Frequency and dysuria persisted and on September 28, 1931, a second cystoscopy showed right ureter normal The left ureter was not definitely seen, but the papillomatous mass had entirely disappeared Now an irregular ulcer was seen on the posterior wall and one behind left ureter Several examinations of the bladder urine after operation were negative for tubercle bacilli Urine became clear and at last the wound began to heal, but the patient developed a psychosis which was considered to be on an arteriosclerotic basis The consultants were not definitely aware of the luetic history

The patient was admitted to the X Hospital on December 8, 1931, and died on December 13, 1931 The diagnosis was general arteriosclerosis, hemorrhage into cerebrum, and postoperative wound following left nephrectomy The laboratory findings just prior to death were urine, 1010, albumin, positive, sugar, none, some white blood cells Blood examination showed hemoglobin, 70 per cent, red blood cells, 3,800,000, white blood cells, 14,000, polymorphonuclears, 76 per cent, lymphocytes, 24 per cent, Van den Bergh, negative, sugar, 105 Blood Wassermann was negative Spinal fluid was clear, smear showed no tubercle bacilli, culture, sterile, albumin, 2 milligrams, globulin, negative, sugar, 100 milligrams

An autopsy was not obtained

A case presenting the classical signs of bladder syphilis is described The patient gave a history of venereal infection, there was evidence of activity as demonstrated by the skin lesions, the blood Wassermann was positive and lesions which could not be accounted for on any other etiological basis were seen to disappear promptly on the administration of antiluetic treatment The patient remained well for a period of about 2 years, the urine continued to be clear and cystoscopy more than a year after the initial examination revealed a normal bladder This set of facts certainly places this case in the category of the many others, most of which were not so thoroughly studied However, subsequent follow-up revealed that the patient actually suffered from renal tuberculosis which was probably complicated by tuberculosis of the bladder It seems reasonable, therefore, to assume that the patient originally suffered from renal tuberculosis complicated by bladder manifestations When these were first brought to the attention of the writer, the patient suffered a concomitant active syphilitic infection Although one would be led to believe that the bladder manifestations were originally syphilitic in the absence of confirmatory bacteriological examinations and animal inoculation, the probability still rests with their being tuberculous There only remains to explain the rapid response to treatment It seems that almost any condition would improve in the presence of syphilis when the latter is treated Furthermore, it is probable that the left urinary tract was temporarily closed off, so that the urinary signs and symptoms would naturally subside This state of affairs is well known to occur in genito-urinary tuberculosis and calycine involvement The operative specimen in this case showed a shut off calyx in the upper pole and active lesions below it

CASE 2 This case was originally reported by Dr Leo Edelman in the *Journal of Urology*, 1928, 20 August.

Fig Cystoscopic appearance of "vegetating syphiloma" described by Corbus and Dunforth (Case 51 in chart) believed by many observers to be typical of bladder syphilis

directly from the floor of the bladder There was no pedicle or frond like appearance There was bulbous edema toward the sphincter The right ureter orifice was normal *and the left ureter orifice could not be seen because of the* vegetating growth Bladder urine was cultured and showed *only a few colonies of Staphylococcus albus and the guinea* pig inoculated with bladder urine showed no evidence of tuberculosis Smears of the centrifuged sediment revealed no tubercle bacilli

A cystogram made on May 28, 1928, showed the great reduction in the bladder capacity which was evidenced by the patient's symptoms The patient was unable to retain more than 1 to ounces of the opaque material, so that an adequate visualization could not be obtained But the left lateral wall of the contracted bladder revealed an irregularity which corresponded to the distribution of the lesion seen through the cystoscope The patient was given antiluetic treatment in the form of neosalvarsan 45 grams on May 19, May 1 and June 5, and an injection of bismuth on May 29

The original blood Wassermann, which was 4+ on May 9, became negative on May 28 and again 4+ on June 4, 1928 *Under antiluetic treatment there was marked and* rapid amelioration of the bladder symptoms so that on May 24 there was only very slight dysuria and the patient was voiding every hour or two throughout the day instead of every half hour and only three times at night On May 24, the skin rash had faded considerably

On May 26, 1928, second cystoscopy was performed by the writer and specimens were removed from the villous masses by means of an operating forceps Unfortunately Levaditi stain could not be made because the specimens were immediately placed in formalin The histopathology showed marked proliferation of the epithelial lining with projections above the level of the bladder mucosa and glandlike inclusions of epithelial elements There was moderate edema with round cell infiltration There was no typical endarteritis, peri vascular infiltration, or areas of focal necrosis The interpretation by Dr Paul Klemperer was "cystitis glandularis

Following the patient's discharge from the hospital, antiluetic treatment was continued *by means of the injections* of neosalvarsan 0 45 grams twice weekly so that she had had eight injections up t July 5 1928, and two injections of mercury salicylat and five of oxycyanide of mercury On this date there was marked improvement in her general condition She looked well, had gained eight and there was no skin rash There was no frequency or urgency and no burning on urination She voided only three or four times during the day and twice at night. The urine was entirely clear Cystoscopy on July 5, 1928, showed several small, irregular elevations about the left ureter orifice These excrescences were much smaller than those seen on primary cystoscopy and were localized above the left ureter orifice only The trigone and right ureter orifice were normal in appearance The bladder capacity was normal

Specimens were again removed for biopsy and these were reported as showing also cystitis glandularis but the later specimens showed more edema and round cell infiltration and foci of large swollen endothelial cells (foam cells) and foci of necrosis

The patient was again seen on December 6, 1928, at which time she made absolutely no complaints There were no bladder symptoms and she was still receiving neosalvarsan and mercury every week with the exception of one month rest The blood Wassermann taken about November was +

On April 15, 1929, there were absolutely no urinary symptoms and the urine was crystal clear Cystoscopy revealed the bladder to be entirely normal Cystogram made on this date showed perfectly normal bladder with normal capacity

Up to this point, a review of the case would leave one with the impression that he were dealing with a well established case of syphilis of the bladder Had the case been reported in 1929 and not followed until the end of 1931 this error would undoubtedly have been made.

The patient was not seen again until the spring of 1931, when she again complained of frequency dysuria, and tenesmus She was not examined but referred to the Mt Sinai Hospital for further study However, she was not admitted immediately and thereupon made the rounds of several hospitals where diagnoses of chronic cystitis and malignancy of the bladder were made

She entered the Mt Sinai Hospital on August 30, 1931 on the service of Dr Edwin Beer and was discharged on November 27, 1931 with the following diagnoses left renal tuberculosis, arteriosclerosis with psychosis and cerebral changes and loss (?) A summary of her stay is as follows Complains of frequency dysuria, and hematuria for 6 months X-ray films of the genito-urinary tract on August 31 1931 revealed normal right kidney left kidney not visualized numerous calcific shadows over both kidneys

Roentgenograms of the chest on August 31 1931 revealed nothing except some cardiac hypertrophy Cystogram on September 1931 was normal. Electrocardiogram on September 1931 showed left ventricular preponderance Cystoscopy on September 1931 by Dr Beer revealed bladder urine to be turbid right indigocarmine excretion was strong Left ureter orifice was retracted, mucosa hyperemic note an extensive polypoid mass, the orifice being congested and patulous Right ureter easily catheterized Left ureter obstructed at 11

Specimens	Bladder	Right	Left
Indigocarmine		Strong	Poor
Microscopic		Negative	Loaded with white blood cells
Sediment for tuberculosis	Negative	Negative	Negative

STATISTICAL SUMMARY OF 158 CASES OF SYPHILIS OF THE BLADDER

Age varies from 6 to 73

	Cases
Sex	
Males	75
Females	64
Not mentioned	19
History	
Positive history of lues or treated for lues	61
No history of lues	89
Active lesions present	28
History of gonorrhea	21
Blood Wassermann	
Positive (+)	83
Negative (−)	22
Not done	53
Cystoscopic findings (Usually a combination of the following lesions was present)	
Ulcers	71
Papules	31
Papillomata	21
Tumors	17
Macules and erosions	13
Cystitis (only)	10
Leucoplacia	5
Fistula	4
Type of treatment	
None	14
Antiluetic (not specified)	67
Arsenicals (usually salvarsan, neosalvarsan or one of these with mercury, bismuth or iodides)	41
Mercury (alone or only with iodides)	22
Iodides alone	6
Bismuth (alone or with iodides)	8
Cystoscopic control following antiluetic treatment	
Controlled	101*
Not controlled	56
Cured	76
Improved	56
Unimproved	8
Died	7

Recurrences specifically mentioned
5 cases, Nos 58, 92, 93, 86, 104

Associated with tuberculosis
Cases 74, 134 Tuberculosis was excluded in only 27 cases by negative smears, cultures or animal inoculation

Histopathology
Reported eight times Only one reported typical syphilitic histopathology Two are claimed to have shown specific pathology, but are not reported in detail The other five cases reporting histology in detail give a description of non-specific inflammation

*Time varied from one day to a few years.

On February 12, 1926, the last cystoscopy performed by Dr Beer showed only some polypoid edema about the sphincter The prostate was moderately enlarged per rectum, patient was voiding three or four times during the day and occasionally once at night and his general condition was good On September 14, 1934, the patient's physician reported that he was in perfect health

The second case is that of a male patient who probably had syphilis about 20 years prior to his first observation when he developed symptoms of cystitis and presented a cystoscopic picture suggestive of neoplasm It was thought that he probably had involvement of the bladder wall secondary to some extravesical disease in the seminal vesicle Specimens excised from the inflamed localized polypoid bladder wall revealed muciparous glands suggesting rectal mucous membrane He responded rapidly to mercury and iodides, but developed a recurrence a year later This time neosalvarsan added to the antiluetic treatment produced a rapid disappearance of the symptoms

SUMMARY

1 A review of the literature since 1900 with an intimate analysis of 158 cases is offered

2 There is a marked laxity in the reporting of cases which are neither thoroughly studied nor followed and adequately controlled

3 Only eight investigators have subjected the lesions to microscopic study Only one shows typical histopathology Two are claimed to have shown specific histopathology, but are not reported in detail The 5 others give descriptions of non-specific inflammation

4 The diagnostic criteria used in most of the cases are described

5 Two cases, one of which possesses all these diagnostic criteria, are described in detail, demonstrating the pitfalls which are encountered in the presence of bladder disease and concomitant syphilis

6 Not one of the cases described measures up to the standard set by Young, who maintains that the spirochæta must be demonstrated in the lesions

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Fig 4 Cystoscopic appearance of the villous papillomatous growth observed by Ajural (Case 55 in chart)

S H male, aged 49 years, private patient of Dr Beer was seen by him April 27 1922, on account of frequency and cloudy urine which had existed for about 10 weeks He had gonorrhea and syphilis in 190 t which time he received antiluetic treatment and has had no symptoms since then, the Wassermann reaction always being negative I addition, he had innumerable prophylactic urethral injections of sulphocarbolate of zinc

Prior to consulting Dr Beer the patient was subjected to cystoscopic examination by another urologist who diagnosed his condition as carcinoma engrafted upon an old syphilis and treated him with radium packs and bladder irrigations Cystoscopy by Dr Beer, April 27 922, showed the anterior and lateral walls of the bladder to be normal, but the floor and trigone were covered with polypoid edema most marked in and about the ureteral orifices and extending well down to the sphincter The whole picture suggested a very intense localized cystitis perhaps due to some extravesical inflammatory focus Several specimens were excised for macroscopic study Rectal examination showed the presence of marked induration about the prostate, possibly due to the effect of the radium packs The physical examination showed no abnormality X ray examination of the genito-urinary tract and cystogram made on May 2, 1922 showed no abnormality The late Dr F S Mandlebaum examined the specimens and reported the following

"Microscopic examination of the specimens removed from S H show edematous and congested bladder wall and numerous small, rounded inclusion epithelial cells of somewhat cystic character I addition there are several areas of glandular acini the cells of which are large and mucinous in nature These glandular elements do not belong to normal bladder structures I t possible that tissue from rectal wall must be considered in identifying the latter? The specimen does not show any evidence of tumor formation in the tissue seen

It was thought from the cystoscopic examination and previous history that the condition was localized hectic disease and in spite of the negative Wassermann, the patient was given mercury and potassium iodide with marked improvement On June 8, 922 the patient had gained 12 pounds, the urine was clear and the frequency had disappeared On that date, the patient was again examined by cystoscope and there was still present bullous edema extending from the neck up over the trigone and posterior wall of the bladder The mucosa in this region was deep red in color containing here and there very evident, white, spherical, minute body To corroborate the macroscopic report, several pieces ere excised The microscopic report by the late Dr F S Mandlebaum on these specimens is as follows

"Microscopic examination of the specimen marked No 1 removed from S H's bladder shows chronic inflammatory process with edema of the submucosa and marked cystic dilatation of the glands Specimen No 2 shows practically the same lesion in addition to some degenerative process in the stroma not unlike any early amyloid change The nodules are almost completely covered with bladder epithelium and represent, in all probability polypoid process of the mucosa due to the action of some chronic irritant All evidence of tumor formation, in the true sense, is absent in all the material examined

After this date the patient remained perfectly ell taking some more mercury and iodides until March 5, 923, *when he presented himself having had recurrence of symptoms* His urine had been cloudy and purulent, his frequency had become very marked, and his bladder capacity much diminished There was throbbing after urination, and although patient looked ery well he had lost much weight His oided urine on this date was bloody and purulent, his capacity as 1 ounce, and it was impossible to cystoscope the patient properly on account of active bleeding There was still marked polypoid edema around the sphincter but no definite tumor was seen By rectum, the right ureter as markedly indurated and the prostate enlarged The urinary examination showed no tubercle bacilli The patient as again put on anti syphilitic treatment with neosalvarsan, his symptoms rapidly disappeared, the urine became clear and he gained about ten or fifteen pounds In the interval between March 5 and March 27 19 3, the patient reported that he had consulted another urologist, who had cystoscoped him and advised operation

On March 27 923, the capacity had increased to 6 ounces and the neck of the bladder seemed almost normal in appearance The posterior part of the trigone and the post trigonal area were occupied by polypoid mass which obscured both orifices As on the first cystoscopy the year before, the lateral and anterior walls were normal The picture suggested an extravesical inflammatory focus ith secondary involvement of the bladder wall It was thought that the condition had primarily begun in a suppurating seminal vesicle with possible perforation of the bladder

On April 4, 1923, the patient again had cystoscopic examination and several specimens ere removed At this examination the polypoid edema was much less marked, but t seemed to be most developed over the position of the right seminal vesicle The urine was clear and rectal examination showed a marked induration abov the prostate The patient at this time was practically normal and had no complaints The microscopic report of the specimens removed t this cystoscopy is as follows

"Microscopic examination of tissue removed from S H's bladder shows marked edema of the subepithelial structures and slight cystic dilatation of the glands There is no evidence in the specimen of the presence of tumor Comparison with previous specimens shows considerably less glandular dilatation and absence of the peculiar mucinous glands

TABULATION OF CASES—Continued

Case	Author	Year Sex Age	History of syphilis or concomitant lesions	Wassermann	Genito-urinary symptoms—duration	Cystoscopic or operative findings	Results of specific treatment and cystoscopic control	Incidental bacteriology histopathology or other laboratory findings
15	3d case	1911 F 47	Paralysis both legs 1 yr 3 abortions in 20 yrs Luetic myelitis		Frequency and dysuria, 1 mo	Large ulcer near left ureter Other ulcers summit and lateral wall 5 cms with papillæ	After antiluetic treatment—slow but progressive improvement. After 2 mos with irrigation—control normal bladder with white scars	Gram positive diplococci, streptococci, no tubercle bacilli
16	Margoulles	1912 F 41	White scars on legs 1 miscarriage			3 excrescences—bean size behind left ureter Diagnosis—carcinoma	Potassium iodide produced rapid improvement 1 mo later control—tumors disappeared leaving insignificant scars	
17	Michailof	1912 F 39		Positive	Hematuria, 5 yrs	Rows of vesicles on lateral and superior wall, each surrounded by red zone	Hemorrhage came from left kidney Bladder symptoms disappeared promptly under antiluetic treatment Control—lesions healed	
18	Mucharinsky	1912 M	1 yr ago—chancre, roseola and treatment			Hyperemia of sphincter, midlobe intruded coin size ulcer on fundus	Complete healing after antiluetic treatment Catheter used for 2 weeks	
19	Picot	1912 M 53	Lues denied Operation—vesical calculi 1 yr later—vesico-rectal fistula	Positive	Hematuria 1 yr frequency, dysuria, 8 yrs.	Left ureter large, gaping Large projections like parquetted floor Plaques with halos and small ulcerations Fistulous orifice ¼ cm	No treatment. No control	
20	Doureoux	1913	No subjective symptoms			Red patches similar to luetic exanthema Lesions seen during routine cystoscopy	Control after antiluetic treatment verified cure	
21	Picker	1913		Negative	Frequency dysuria	¼ cm yellow prominence near right ureter	Complete healing after antiluetic treatment	
22	Gayet and Favre 1st case	1914 M 66	Tabetic	Positive	Hematuria frequency dysuria, 15 mos	Median lobe enlarged with ulcer over median lobe 2 other ulcers near left ureter covered with papules	After 6 mos weekly calomel and potassium iodide ulcers healed Hematuria disappeared at beginning of treatment	
23	2d case	1914 F 55	Lues denied 7 yrs ago had sudden perforation at juncture of hard and soft palate		Hematuria, frequency, dysuria sudden	Numerous papillomata with cerebral convolutions	Arsphenamine begun before bladder visualized 5 days later papillomata seen Later only ridges seen	
24	3d case	1914 F 35	11 yrs ago chancre of lip		Hematuria frequency, dysuria, 15 days	Trigone red with median projection (like prostate), Sphincter red	Simple rubbing brought about complete cure	
25	Shapira	1915 M 46	Chancre 17 yrs. ago and discharged as cured 15 yrs later rash diagnosed as luetic Wassermann became negative 2 yrs ago after 5 arsphenamine when rash disappeared After 1 injection arsphenamine Wassermann became positive	Positive	Frequency, dysuria, 5 mos	Slight congestion, very trabeculated Ulcerated patch 2 cms near left ureter and another smaller one nearby	After mercury and potassium iodide and local treatment, bladder symptoms disappeared and control showed normal bladder and negative Wassermann	
26	Pedersen 1st case	1916 M 71	Lues 50 yrs with only oral medication Finally cured 10 yrs ago with intensive treatment		Hematuria, frequency dysuria, 5 yrs	Retention Cystoscopy—difficult Diagnosis neoplasm (?)	Antiluetic treatment only partial success After 1 mo fleshy mass with villous formation and necrosis. 9 mos after antiluetic treatment bladder improved	

TABULATION OF CASES

Case	Author	Sex Race Age	History of syphilis or concomitant lesions	Wassermann	Genito-urinary symptoms—duration	Cystoscopic or operative findings	Results of specific treatment and cystoscopic control	Incidental bacteriology, histopathology or other laboratory findings
	Matzenauer	[illegible]	Lues 4 years			Papillomas like projections resembling villus tuft. Ulcer on superior wall of urethra	None	
	MacGowan	[illegible]	Lues, 10 years			Papillomas like projections behind right ureter. Concretions adherent with hard substituted edges	None	
	LaFur	[illegible]	Lues, 6 years. Treated irregularly. Developed lesion patch on the pharynx while under observation		Hematuria years	3 ulcers on trigone	After antiluetic treatment—complete recovery in short time. Control—whole years. Irregular hard nodule in prostate became normal after antiluetic treatment	No gonococci. No bacteria in urine
4	Graff	[illegible]	Painless doughy swelling of both testicles			Tumor like growth with central defect and papillary proliferation at edges. Suprapubic operation—ulcer enlarged	6 weeks after operation and antiluetic treatment discharged cured	Excised tissue—chronic necrotic cell masses and bladder epithelium which did not show tumor formation
5	Asch yet cases	[illegible]	Ulcer on labium, 3 mos ago. Inguinal glands hard, enlarged and painless			Scattered superficial round defects with whitish lesions like lactic patches	Ulcer after mercury intramuscular symptoms began to improve 4 [illegible] later 3 injections almost gone, bladder showed slight red spots, 6 wks later bladder normal. 3 yr later control also normal	No tubercle bacilli in urine by microscopic or inoculation
6	yet cases	[illegible]	Lues, 20 yrs before. Hardly any treatment			Papillary and ulcer surrounded by papillae		No gonococci or tubercle bacilli
7	yet cases	[illegible]	Chancre 20 yrs ago. Treated superficially. Ulcer on right thigh 3 mos			Large granulomatous ulcer on fundus	4 days after symptomatic ulcer on thigh and bladder symptoms disappeared and control showed normal bladder	
8	Paraschevin yet cases	[illegible]	Luetic lesions on skin and mucous membranes			Several ulcers near left ureter	Mercury injections produced rapid amelioration of symptoms	
	yet cases	[illegible]	Luetic lesions on skin and mucous membranes			Several small ulcers in prostate	Mercury injections produced rapid amelioration of symptoms	
10	yet cases	[illegible]	Luetic lesions on skin and mucous membranes			Small ulcerations scattered all over bladder sphincter adenomatous	Mercury injections produced rapid amelioration of symptoms	
	Pertuiss	[illegible]	Lues, 10 yrs. Cutaneous gummata		Hematuria 14 mos	Granulomatous ulcer	After antiluetic treatment, lesions [illegible] mos. Later control—complete cure	No tubercle bacilli
	Halmovits	[illegible]		Positive		Large granulomatous ulcer on trigone and tumor on lateral wall	10 days after symptomatic ulcer disappeared and tumor was reduced to small size	
13	von Engelmann yet cases	[illegible]	No luetic history (See Lehmann 7)		Hematuria, 6 mos. no frequency or dysuria	Tumor on ureter. Ureter with ulcer and surface disappeared in cicatrices	Later determined patient had lues 20 yrs ago. Ulcers healed rapidly under mercury and tumor disappeared in few wks	
14	yet cases	[illegible]	Lues 3 yrs ago. Mercury and [illegible] iodide. Paralysis left leg [illegible] yr. Disappeared after mercury		Hematuria, [illegible]	Round tumor located near ureter right kidney with ulcerated surface and papillary changes	After 30 mercury injections tumor disappeared and red spot was found in chest plate	

TABULATION OF CASLS—Continued

Case	Author	Year Sex Age	History of syphilis or concomitant lesions	Wassermann	Genito urinary symptoms—duration	Cystoscopic or operative findings	Results of specific treatment and cystoscopic control	Incidental bacteriology, histopathology or other laboratory findings
40	Wallace 8 cases Corbus 1st case	1918 M 28	No luetic history Pain in kidney and bladder 3 yrs ago		Hematuria, frequency, dysuria 6 mos.	Prostate enlarged Villous growths on right near sphincter—others near right ureter	Antiluetic treatment followed by complete cure and disappearance of growth	
41	2d case	1918 F 43	No luetic history 1 miscarriage 1 stillbirth	Positive	Hematuria, frequency dysuria	Papules and ulcer on internal sphincter 3 irregular ulcers on trigone, resembled tuberculosis	Lesions cleared up under antiluetic treatment	
42	3d case	1918 M	No luetic history Father had lues 30 yrs ago Congenital lues presumed	Positive	Hematuria, frequency, dysuria	Ulcerated and nodular trigonitis Ulcer and few nodes on internal sphincter	Lesions cleared up under antiluetic treatment	
43	4th case	1918 F 30	No luetic history Operation on kidney Bladder symptoms 11 yrs	Positive	Frequency dysuria, 11 yrs	2 ulcers near right ureter several near left ureter 4 on trigone Papules and ulcers about internal sphincter	Patient became apparently well under antiluetic treatment	
44	5th case	1918 F 28	No luetic history Referred for cystitis	Positive		Papules and ulcers on trigone and near right ureter and sphincter	Fulguration and bladder irrigation unsuccessful Healed under antiluetic treatment	
45	6th case	1918 M 40	No luetic history Suprapubic cystotomy 3 yrs ago for growth	Positive	Frequency dysuria 3 mos	Ulcer of base and trigone Very inflamed bladder	2 injections of arsphenamine and other antiluetic remedies produced great improvement	
46	7th case	1918 M 29	Gonorrhea 12 yrs ago Operation 2 yrs ago for stone None found Papilloma removed	Positive		Ulcerations and villous growth of neck extending to trigone	Under intensive antiluetic treatment growth disappeared and bladder cleared	
47	8th case	1918 M 29	Gonorrhea 14 yrs ago and recently Large prostate and stricture of urethra	Positive	Frequency dysuria	Thickened bladder with distinct gumma near left ureter	Results of treatment not recorded	
48	Denslow	1918 M 23	Chancroid 2 yrs ago Gonorrhea 1 yr ago continued to date of examination	Positive	Frequency dysuria, 1 yr	Papillomatous masses in posterior urethra and around sphincter Operation-condyloma like nodules studded base of bladder Nodules curetted	Under mixed treatment, normal conditions in 3 mos	Curettings reported "syphilitic condyloma"
49	Cole	1918 F 34	Treated for lues 12 yrs ago Gonorrhea twice 8 and 10 yrs. ago	Positive	Hematuria 2 yrs Frequency, dysuria, 6 yrs	Severe trigonitis with edema Large crescentic ulcer near right and left ureters	Improved under arsphenamine and mercury 3 mos later control—white scars. 3 yrs later no symptoms	
50	Hesse	1918 F 24	Lues denied Tuberculosis in family	Positive	Frequency, dysuria	Reddish brown circular papules in fundus	Recovered under antiluetic treatment No control	No tuberculosis
51	Ringleb	1919 F			Frequency, dysuria	Ulcer with craterform edge infiltrating rectum and genitalia	Under iodides condition improved No control	
52	Dansforth and Corbus	1920 F 25	Gonorrhea 3 yrs ago Criminal abortion followed by fever Vesicovaginal septum infiltrated	Positive	Frequency, dysuria, 2 mos	Infiltrated growth with many peaked projections of papillomatous character suggesting malignancy Operation—cystotomy lesion on base not malignant	2 wks after antiluetic treatment control—improved 2 mos later wound healed general condition good No further control	Gonorrhea and tuberculosis negative
53	Thompson	1920 M 25	Ulcer of penis 3 mos ago Typical roseola and adenitis 3 days No treatment	Positive	Hematuria, frequency dysuria, 2 days	Trigone congested Ulcerating papules near each ureter	Hematuria ceased 1 day after 1 arsphenamine and mercury 4 wks after 4 arsphenamine and mercury—no symptoms and control—normal bladder	No spirochætæ found in urine on dark field

TABULATION OF CASES—Continued

No.	Author	Sex Age	History of [illegible] or congenital lesion	Urinary results	Genito-urinary symptoms—duration	Cystoscopic or operative findings	Results of specific treatment and cystoscopic control	Incidental bacteriology, histopathology or other laboratory findings
[illegible]	Rouchal	[illegible]	No history of lues. Symptomatic of cystitis	Positive		Er [illegible] papules	Antiluetic treatment produced rapid cure	
[illegible]	Schlechter and Lutzenkott	[illegible]	History of lues treated years before yrs ago		Frequency, dysuria	[illegible] papules [illegible] of bladder with red halo	No treatment—no control	
[illegible]	Cicchetto	[illegible]	Lactic constitution	Positive	Frequency, dysuria, few wks	Yellowish papules with red halo near ureters	1 day after neosalvarsan halos begin to disappear [illegible] after mercury ribs, papules disappeared	Gonococci [illegible] Pyogenic organisms Various bacteria in urine
[illegible]	[illegible] case	[illegible]	Gonorrhea [illegible] and [illegible] yrs ago No lesion history	Positive	Hematuria, frequency, dysuria, 8 yrs	[illegible] days after initiation of antiluetic treatment observed congestion of mucous membrane	After 4th injection of mercury symptoms were relieved and [illegible] later symptom free 7 mos later completely cured	Rare diplococci and gram positive bacteria in sediments No gonococci or tubercle bacilli Y ray negative
[illegible]	[illegible] case	[illegible]	Abortion No gonorrhea or tuberculosis	Negative	Hematuria, frequency, dysuria, 14 yrs	Ulceration	After [illegible] neosalvarsan and mercury [illegible] marked improvement and control showed lesions almost healed [illegible] after antiluetic treatment—control and third cystoscopy showed only scar. Stopped antiluetic treatment and retested [illegible] later—4th cystoscopy showed ulceration. Mercury [illegible] and neosalvarsan started and 10 days later 4th cystoscopy almost healed lesions [illegible] after antiluetic treatment—symptom free and 6th cystoscopy—entire scar	No gonococci or tubercle bacilli
[illegible]	H. Parker	[illegible]	Gonorrhea [illegible] yrs ago and [illegible] yrs ago Left orchidectomy and right epididymitis. Treated for lues small [illegible] ago with mercury [illegible] ago with neosalvarsan [illegible]		Frequency dysuria	Small yellowish projections with red halo Papules on left lateral wall days later yellowish spots below After [illegible] nodule about developed at site of papules	days later all lesions showed beginning healing [illegible] after six cystoscopy lesions almost healed	
[illegible]	Pasteur case	[illegible]	abortion Husband treated for lues	Positive	Frequency dysuria, yrs	Small gray-ish papules and nodules [illegible] red halo	After neosalvarsan several controls showed normal bladder and no symptoms	
[illegible]	[illegible] case	[illegible]	abortions and premature [illegible] years	Positive	Frequency dysuria, yr	Many gray-ish white papules with red halo on trigone and interureteric ridge	3 hr after neosalvarsan and mercury marked improvement in symptoms and control—most of papules disappeared 3 mos later after complete course—no symptoms and control—normal except for leucoplakia	
[illegible]	Ohnes and Pessier	[illegible]	6 lactations	Negative	Hematuria frequency dysuria	Ulceration	[illegible] days after neosalvarsan symptoms gradually improved and bladder almost normal	
[illegible]	Pasteur	[illegible]		Positive	Frequency dysuria	Cystitis and small ulceration	Healed under antiluetic treatment	
[illegible]	Ehrlich	[illegible]		Positive	Hematuria frequency dysuria	Ulcer	Healed under antiluetic treatment	

TABULATION OF CASES—Continued

Case	Author	Year Sex Age	History of syphilis or concomitant lesions	Wassermann	Genito-urinary symptoms—duration	Cystoscopic or operative findings	Results of specific treatment and cystoscopic control	Incidental bacteriology, histopathology or other laboratory findings
*65	Perucci	1922		Positive	Hematuria, frequency, dysuria	Granulomatous ulcer	Healed under antiluetic treatment	
*66	Beuc	1923		Positive	Hematuria frequency, dysuria	Ulcer	Healed after 4 neoarsphenamine	
*67	Uras	1924		Positive	Frequency, dysuria	Ulcer	Healed under antiluetic treatment	
*68	Cirillo	1924		±	Frequency dysuria	Appearance of tertiary lues	Healed under antiluetic treatment	
*69	Aranda	1924				Roseola	Healed under antiluetic treatment	
*70	Girard 1st case	1925	Cumma cubiti	Positive	Frequency dysuria	Ulcers and cystitis	Healed under antiluetic treatment	
*71	2d case	1925		±	Dysuria	Macules and mulberry appearance		
*72	3d case	1925		±	Dysuria	Macules and mulberry appearance		
73	Coll	1925	Lues			Appearance of cystitis and gumma	Healed under antiluetic treatment	
74	A Peterson 1st case	1924 M 45	Gonorrhea 19 yrs ago No luetic history	Positive	Frequency dysuria, 8 mos	Diffuse cystitis with edematous area Suprapubic cystostomy revealed ulcer	Neoarsphenamine and mercury for 5 wks and discharged from hospital without improvement Died 3½ mos after operation Diagnosis—pulmonary tuberculosis	No tubercle bacilli in urine
75	2d case	1924 F 29	Pain over right kidney, red blood cells in urine and X ray film showed suspicious shadow over right kidney	Positive		2 ulcers near right ureter which could not be catheterized	Ascites. Diagnosis of lues of bladder right kidney and liver Severe reaction after arsphenamine After 25 mercury felt well No ascites no control	No tubercle bacilli in urine
76	Luttichau	1925 F 19	Treated for cystitis for a long time	Positive		Inflamed bladder	After antiluetic treatment symptoms and signs disappeared	
77	DeGouvea 1st case	1924 F 60		Negative	Frequency dysuria	Lobulated tumor	15 days after antiluetic treatment marked improvement. 5 wks after mercury and iodine no symptoms and control—scar and normal bladder	
78	2d case	1924 M 34	Left renal colic and hematuria X ray showed no calculus but left kidney larger		Hematuria	Small red spot with superficial ulceration	Antiluetic treatment cured him	No tubercle bacilli
79	3d case	1924 M 32	No venereal history	Negative	Hematuria, frequency, dysuria	Irregular tumor surrounded by red zone	Treated with mercury and iodides and later learned that he was cured	
80	4th case	1924 M 32	Gonorrhea and chancre 5 years ago		Frequency, dysuria	Irregular whitish gray spots	All symptoms disappeared after antiluetic treatment and control showed normal bladder	
81	5th case	1924 F 55			Frequency, dysuria, 1½ 3 yrs	Sessile tumor Suprapubic cystotomy 12 days later revealed tumor over trigone	40 days after neoarsphenamine and iodides—cured and control showed normal bladder	Chronic inflammation—no sign of malignancy No mycosis

*Cases 62 to 72 inclusive are cited by Chocholka in 1926

TABULATION OF CASES—Continued

Case	Age	Year of Age	History of trouble before treatment	Wassermann	Urine examination	Cystoscopic findings	Results of specific treatment and present condition	Incidental but interesting history, final diagnosis and other pathologic findings
3	4th case	[illegible]	Left renal [illegible]	Negative	Hematuria, frequency, dysuria	Large irregular tumor bleeding easily	[illegible] day after antiluetic treatment tumor smaller [illegible] later—large scar at site. No recurrence	
13	7th case	[illegible]	Tubercle [illegible]		Hematuria, frequency, dysuria	Red tinted areas with hypertrophy and [illegible]	Antiluetic treatment with [illegible]. Almost complete disappearance of [illegible] tumor. Later control—normal bladder	
14	8th case	[illegible]	Operation for [illegible]	Negative		Red lesion [illegible] with [illegible] and [illegible] changes	[illegible] after antiluetic treatment control—normal bladder	
	9th case	[illegible]	No luetic history. Right renal colic. [illegible] very small [illegible]		Hematuria, frequency, dysuria	Ureteral [illegible] right ureter. Check [illegible]	Rapid relief after [illegible], mercury and iodides. [illegible] later control—scar [illegible] of ureter	
15	Spelled	[illegible]	Consultation [illegible] yrs. ago [illegible]	Positive	Hematuria, frequency, dysuria, pus	Small lesion in bladder [illegible] small deep ulcers	[illegible] after mercury, iodide and neosalvarsan [illegible] improved. [illegible]	Ulcerative [illegible] through [illegible] later healed by [illegible] marked [illegible] [illegible]
	Lucy	[illegible]	Two abortions	Positive	Frequency, dysuria	[illegible] small lesion [illegible]	After [illegible] injections mercury and [illegible] well. After [illegible] control—well [illegible]	[illegible]
11	Rarities	[illegible]	Consultation [illegible] yrs. ago [illegible]	Positive	Hematuria, frequency, dysuria, [illegible] days	[illegible] white small papules with red halos	Hematuria disappeared after [illegible] injections. After [illegible] control—normal bladder	
16	Blanc and Jerry	[illegible]	Treated many years for [illegible] passed gas from urethra [illegible]	Negative	Frequency, dysuria, [illegible]	Vesico-intestinal fistula, shown by cystoscopy and cystogram	After all injections of bismuth and [illegible] [illegible] yr. later after continued antiluetic treatment control—only slight [illegible]. Cystogram—no fistula. No recurrence	
10	3d by [illegible] case	[illegible]	Consultation [illegible] yrs. ago. Over [illegible] years under [illegible] and personal [illegible] 4 yrs. ago	Positive	Hematuria, frequency, dysuria	Ulcerations in deep urethra, dilated prostatic [illegible] by [illegible] days later red [illegible] but [illegible] with small capacity and several ulcers	After [illegible] weeks antiluetic treatment symptoms [illegible] later [illegible] control—ulcers healed [illegible] later control—normal bladder with scar	
12	2d case	[illegible]	Chancre [illegible] yrs. ago	Positive	Frequency, dysuria, [illegible] days	Elongated ulcer near left ureter	Hematuria ceased after [illegible] injections. No control cystoscopy	
10	Antonetta	[illegible]	Treated for [illegible] yrs. ago. No history of gonorrhea	Positive	Hematuria, frequency, dysuria, few days	Small ecchymotic area and small ulcer near [illegible]	Symptoms subsided after [illegible] injections [illegible] later control—normal. [illegible] later [illegible] symptoms but no control [illegible] later [illegible]	No gonorrhea in urinary sediment

TABULATION OF CASES—Continued

Case	Author	Year Sex Age	History of syphilis or concomitant lesions	Wassermann	Genito-urinary symptoms—duration	Cystoscopic or operative findings	Results of specific treatment and cystoscopic control	Incidental bacteriology histopathology or other laboratory findings
93	Rothschild	1926 F 67	No gonorrhea Husband luetic	Negative Later ±	Frequency, dysuria, 6 mos	Papules with condyloma like lesions with red halo 1 mo after irrigation with silver nitrate, only 2 papules remained These papules persisted until 4 mos. later when they were coagulated with high frequency	Symptoms returned in a few wks. and control—8 mos after 1st cystoscopy—same findings 1 mo after silver papules disappeared again Patient not seen for 7 yrs returning with frequency and dysuria 3 wks. Well in 7 years' interval Last cystoscopy showed dark red patches	
94	Molina 1st case	1927 F 30	No venereal history	Positive	Hematuria, frequency dysuria	Ulcers	3 wks after 6 injections of iodo-bismuth control—normal bladder	
95	2d case	1927 F 26		Positive	Hematuria frequency dysuria 3 mos	Ulcers resembling tuberculosis	After iodo-bismuth control—scar in normal bladder	
96	3d case	1927 M 73	Old luetic treated only with mercury Renal colic with passage of small stones. Incomplete retention due to prostate		Hematuria frequency dysuria	3 vesical calculi superficial ulcers and cystitis Litholopaxy followed by lavage but symptoms continued	After 4 iodo-bismuth improvement in all symptoms After 15 injections control—normal bladder	
97	Gautier	1927 M 44	Lues 9 yrs with rectal ulcers Treated for 5 yrs No treatment in last 4 yrs. Infiltration above prostate	Positive		Gummatous ulcer with crateriform edge Several petechial spots	1½ mos after 12 bismuth and 6 stovarsol—no symptoms, no rectal infiltration and control—normal bladder	
98	Papin	1927 M 44	Chancre 9 yrs. ago Treated 2 yrs Wassermann negative No treatment since Large left testicle Right kidney large and tender X ray negative	Positive	Hematuria 1 yr Frequency, dysuria, 3 mos	Number of lentil size papules 30 days after mercury oxycyanide and 2 neoarsphenamine per week testicle smaller, right kidney smaller, urine clearer, and control—papules fading	10 mos with mercury and potassium iodide all symptoms subsided and considered cured	
99	Turner 1st case	1927 M 64	Suprapubic cystotomy for bladder ulcer 10 yrs ago No luetic history Large boggy prostate Retention 4 mos.	Positive	Hematuria, 4 mos Frequency, dysuria, 10 yrs	Solitary ulcer found on suprapubic cystotomy Diagnosis—cancer	Under antiluetic treatment hematuria subsided and ulcer healed 3 wks later 2d stage prostatectomy—uneventful recovery 6 wks later control—normal bladder 6 yrs. later slight frequency and dysuria cured by dilatation	
100	2d case	1927 M 52	Symptoms followed appendectomy with drainage and catheterization Prostate large, boggy, tender Vesicles nodular	Positive	Hematuria and frequency 1 yr	No residual Red and edematous mucous membrane Ulcer near left ureter	Symptoms improved under antiluetic treatment but patient died 2 years later—cause unknown	
101	3d case	1927 M 61	Chancre 8 yrs ago, no treatment. Prostate large, boggy, indurated area Right seminal vesicle Retention ½ ounce	Positive	Hematuria, frequency, dysuria, 2 yrs	Prostatic ring contracted Mucous membrane red and edematous Ulcer with papillomatous nodules	No symptoms 2 mos after antiluetic treatment No control	
102	4th case	1927 F 29	No luetic history	Positive	Frequency, dysuria, 1 yr	Ulcer with bullous edema	5 wks after antiluetic treatment control—ulcer healed Slight congestion No symptoms	
103	5th case	1927 F 51	No luetic history Hysterectomy for tumor 10 yrs. ago Never pregnant Mild kraurosis Band like constriction in adnexal region rigidly holding base of bladder	Negative later positive		Ulcer with bullæ	2 mos after antiluetic treatment greatly relieved except small bladder capacity	

TABULATION OF CASES—Continued

Case	Author	Year Age Sex	History of syphilis or concomitant lesions	Wassermann	Cystoscopy or operative findings	Cystoscopic or operative findings	Results of specific treatment and cystoscopic control	Incidental bacteriology histopathology or other laboratory findings
[illegible]	6th case	[illegible]	No luetic history	Positive	Hematuria 18 mos.	Pap. hemorrhagic tumor with bleeding from right ureter	3 wks after antiluetic treatment hematuria ceased [illegible] later much improved, control—normal bladder. Returned [illegible] later with positive W. [illegible] and some cystoscopic picture. Now under anti luetic treatment	
[illegible]	Pugh not case	[illegible]	Lues 10 yrs. ago treated [illegible] Hard prostate. Treated with iodide	Positive	Hematuria frequency dysuria	Relaxation of sphincter. Superficial ulceration and small growths, also prostate in prostatic urethra	Marked improvement in 3 mos. under antiluetic treatment. Then patient disappeared	Tissue taken from growths reported as syphilitic
[illegible]	[illegible] case	[illegible]	Lues and lumbar vertebrae. Repeated telangiectasia for bladder [illegible]	Positive	Hematuria, frequency dysuria, 4 yrs.	Papillomas like [illegible] near right ureter	Apparent subsidence of all symptoms under antiluetic treatment	Section taken from [illegible] reported syphilis
97	[illegible] case	[illegible]	General adenopathy, especially epitrochlear. Based like hard [illegible] of blood for much per vagina	Positive	Hematuria frequency dysuria,	Large area suggesting cystitis cystica, found to be pedular on attempting puncture—no fluid obtained	Under antiluetics and bismuth local condition improved satisfactorily	
[illegible]	4th case	[illegible]	Treated 10 yrs. ago for lues irregularly	Positive	Hematuria frequency 6 mos. 1 yr.	Engorgement of bladder. Several small hard like ulcers near both ureters	Under antiluetics, mercury and bladder irrigations condition cleared readily	
[illegible]	5th case	[illegible]	Treated for penile lesions 10 yrs. ago and admitted syphilis [illegible] ago. Prostate and vesicles tender	Positive	Frequency, dysuria mos.	Ulcers on trigone between ureters may posting cancer	Placed on antiluetic treatment. He was doing well but has disappeared	
70	A. A. Palmer not case	[illegible]	Several abortions		Hematuria, frequency dysuria, mos.	Several elevated red nodal tumors near right ureter and lesions resembling tuberculosis	After 10 mercurial control—normal bladder. Ulcer of cervix healed	No tuberculosis in urine. No tubercle bacilli. Gonococci neg. negative
	and case	[illegible]	Operation for inguinal hernia		Frequency, dysuria	Slight enlargement of prostate producing slight retention. Ulcers on trigone	Mercury resulted in cure. No control	
	3rd case	[illegible]	Urethral discharge many years in spite of negative smear		Frequency, dysuria	3 ulcers near right ureter and lesser ulcerated spots on trigone	Cured with 10 injections of mercurial. No control	
	4th case	[illegible]	Chancre 3 yrs. ago. Gonorrhea 10 yrs. ago. Treated for gleet [illegible]. Better for gonococci, [illegible]			Ulcers on trigone	After 914 and mercurial urine cleared, no symptoms and control—normal bladder	
4	5th case	[illegible]	Tabetic crises (?)		Hematuria, frequency dysuria, 3 mos.	ecchymotic areas	Hemorrhagic cystitis resulted in complete cure. No symptoms. No control	
5	6th case	[illegible]	Lues denied. Pregnant [illegible] mos.		Hematuria frequency dysuria, yrs.	Deeply congested mucous membrane of entire bladder	Improved after [illegible] mercury salicylate. After neosalvarsan hematuria, frequency dysuria disappeared and control hyperemic areas	
78	Nitzki not case	[illegible]	No luetic history	Negative	Hematuria, frequency dysuria, yr.	Inland not elevations on trigone. Open lesion hemorrhagic removed and ulcers discovered. Tuberculosis and other [illegible]—no effect	Potassium iodide produced prompt relief. 14 mos. later control—normal bladder and hyperemia at ulcer sites	

TABULATION OF CASES—Continued

Case	Author	Year Sex Age	History of syphilis or concomitant lesions	Wassermann	Genito urinary symptoms—duration	Cystoscopic or operative findings	Results of specific treatment and cystoscopic control	Incidental bacteriology histopathology or other laboratory findings
117	2d case	1928 F 47	No luetic history	Positive	Frequency dysuria, Sev 3 yrs.	Several yellowish elevations on trigone	3 wks after antiluetic treatment symptoms disappeared and control—normal bladder	
118	K Ries 1st case	19 8 M 6	Periodic hematuria 1½ yrs Father luetic. Elder brother blind	Positive	Hematuria frequency, dysuria, 1½ 3 yrs.	None	Hematuria subsided after mercury inunctions in several wks No symptoms after several mos.	
119	2d case	1928 M 45	Headaches, cachexia and anemia Unequal pupils and red optic discs	Positive	Hematuria 15 3 yrs	Gummatous ulcer near left ureter Tumor extends over trigone 3 cms	Under mercury inunction and arsphenamine, hematuria disappeared in several wks Control—normal bladder	No tubercle bacilli No gonococci
120	Chocholka 1st case	1928 F 42	Many abortions Peration fibroid uterus 1 yr ago			Papillomata on posterior wall Electrocoagulation painful and without effect	2 mos after antiluetic treatment symptoms disappeared control—scar	
121	2d case	1928 M 45	Diabetes and nervosite No luetic history		Hematuria frequency dysuria	Trabeculated hypertrophy with incrustation surrounded by inflamed mucous membrane and pseudo membrane	Succumbed to peritoneal crisis before operation was possible Diagnosis—paresyphilis	
122	3d case	1928 F 39	Many miscarriages No gonorrhea	Positive		Ulcerating gumma on posterior wall	None	No tubercle bacilli No gonococci
123	4th case	1928 F 27	Many miscarriages	Negative		Pseudo-membrane and ulcerative cystitis No improvement with local treatment. 2nd and 3rd cystoscopic examination 1 yr later showed papules	1 mo after antiluetic treatment cure was obtained with control cystoscopy	
124	5th case	1928 M 58	Bilateral orchitis 2 yrs	Negative		Fistulous orifice ½ cm near right ureter with pus escaping	Under antiluetic treatment his physician reported clear urine	No tubercle bacilli No gonococci
125	6th case	1928 F 36	Lues 10 yrs Many miscarriages in recent years	Negative		Brownish red areas surmounted by yellowish papules of lentil size	Exclusive antiluetic treatment produced disappearance of all lesions	
126	7th case	1928 M 31	Cystitis since gonorrhea 7 yrs ago Local treatment failed	Positive		Ulcer with pseudo-membranous cystitis and yellowish papules on trigone	6 mos. after antiluetic treatment no symptoms and control—normal bladder	No tubercle bacilli No gonococci
127	8th case	1928 F 35	Treated 20 yrs. ago for lues. 3 miscarriages since Dry papules on leg	Positive		Aspect de mure	After 4 neoarsphenamine papules on leg disappeared and no symptoms 2½ mos later control—normal	No tubercle bacilli No gonococci
128	9th case	1928 M 39	Rebellious gonorrhea 6 yrs	Negative		Ulceration on trigone	After 1 injection—improvement After 4 injections no symptoms and control—normal bladder	No tubercle bacilli No gonococci
129	10th case	1928 M 61	Lues 20 yrs ago Denied gonorrhea or tuberculosis Neurologic examination did not exclude lues	Negative 3 yrs positive		Hypertrophy left lobe of prostate Small miliary elevations over mucous membrane	After 6 bismuth all symptoms disappeared Patient refused control	
130	11th case	1928 M 43	Gonorrhea 18 yrs ago with stricture 12 yrs. Treated for lues and cystitis	Positive		Bullous edema of sphincter with small yellowish and red elevations about left ureter	After 3 bismuth all symptoms disappeared and control—normal bladder	No tubercle bacilli No gonococci

TABULATION OF CASES—Continued

Case	Author	Year Age	History of syphilis or concomitant lesions	Wassermann	Genito-urinary symptoms—duration	Cystoscopic or operative findings	Results of specific treatment and cystoscopic control	Incidental bacteriology histopathology or other laboratory findings
11	Lenzmann not cited	1908 F 36	Miscarriage. Husband indicated syphilis and treated for syphilis	Positive	Hematuria, frequency, dysuria, pus	Small capacity. Cystitis with red ulcers from inner right ureter	[illegible] mos. after nonsymptomatic symptoms disappeared and control—normal bladder 6 mos. later no symptoms	
12	Ad cited	1909 F 48	Lesion vagina and pelvic adenopathy—syphilitic	Positive	Hematuria, frequency, dysuria, pus	Disorganized papillae with macules on enlarged bladder base	After antisyphilitic treatment vaginal lesions and symptoms subsided; yet control—macules disappeared. After 20 injections and 3 nonsymptomatic control—normal bladder	
13	Bennett and Cotton	1908 F	Small vesicovaginal fistula	Positive		Lateral one lesions surrounded by red halo—lesions purple. Fistula seen	After antisyphilitic treatment lesions disappeared and fistula closed	
14	Marks and Miller	1909 F 34	Vesicovaginal fistula. X ray chest suggestive of pulmonary tuberculosis. Spinal fluid negative	Positive	Hematuria, frequency, dysuria, 6 mos.		After 3 mos. of non-specific treatment with no improvement, antisyphilitic treatment with mixed treatment was begun followed by nonsymptomatic. After mos. marked improvement in genitalia tract and free from pus. Following teeth abscess—pneumonia—death.	Biopsy of fistula showed typical tubercles with characteristic giant-cells and tubercular granulations
15	Gordon not cited	1909 F 35	Miscarriages	Positive	Frequency, dysuria	Whitish exudate over trigone with hyperemic areas	No result after mos. irrigations. After 6 nonsymptomatic and silver nitrate irrigations symptoms disappeared and areas clapped. No control	
16	Ad cited	1909 F 30	No history of lues	Positive		Ulcers on trigone and ulcer near left ureter	After 6 daily mercury oxycyanide and irrigations symptoms disappeared and 20 days later control—normal	
17	Ad cited	1910 F 34		±		Bladder uniformly congested with bed from edema. No ulcers	After 3 nonsymptomatic—improved. After 30 injections control—slight congestion of trigone	
18	4th case	1910 F 36	Old gonorrhea	Negative		Large ulcers behind trigone	[illegible] after mercury oxycyanide control—complete cure	
19	Rasmussen not cited	1910 F 40	Abortion. Lesions skin, mucous, deep ulcerations of vulva and genitalia, with ulcer at vesical sphincter	Positive	Hematuria, frequency, dysuria, pus	After [illegible] days of antisyphilitic treatment cystoscopy possibly infiltration hyperemic areas with multiple superficial and deep ulcers on trigone	Control on 16th, 20th and 25th days after mercury oxycyanide showed regression of lesions. Frequency, dysuria, disappeared on 5th day and hematuria on 30th day	No tubercle bacilli or gonococci. No other bacteria

TABULATION OF CASES—Continued

Case	Author	Year Sex Age	History of syphilis or concomitant lesions	Wassermann	Genito-urinary symptoms—duration	Cystoscopic or operative findings	Results of specific treatment and cystoscopic control	Incidental bacteriology, histopathology or other laboratory findings
140	2nd case	1930 F 37	Husband had chancre at 21 yrs. of age. Treated irregularly No pregnancy in 15 yrs	Positive	Hematuria, frequency, dysuria, 15 days	None	After 10 days irrigations and mercury oxycyanide for 12 days—symptom free	
141	3d case	1930 F 18	Lesion on genitalia Ulceration at meatus and superficial ulcer of labia Macular skin eruption		Frequency dysuria, 1½ mos	Superficial ulceration on trigone	After 3 neoarsphenamine skin and labial lesions disappeared 21 days after 5 neoarsphenamine all lesions healed and control—normal bladder	
142	4th case	1930 M 43	Chancre 20 yrs ago with irregular treatment	Positive	Hematuria, frequency, dysuria 8 mos	Gummatous ulcer on lateral wall	Cured rapidly in 18 days on antiluetic treatment. No control	No bacteria
143	5th case routine observation	1930 F 38	Chancre 45 days. Strong roseola No treatment		Frequency dysuria, 4 days	6 papules on trigone 36 hours after 1st arsphenamine color increased Herxheimer	On 20th day of treatment, control—normal bladder	
144	6th case routine observation	1930 F 31	Chancre 6 mos Papules on abdomen and vulva		None	Papules with hyperemic halo	At the end of series of arsphenamine control—normal bladder	
145	7th case routine observation	1930 F 35	Chancre 4 mos Papules on abdomen		Frequency dysuria	Ulcer	After 1 mo antiluetic treatment control—no ulcer	
146	8th case routine observation	1930 M 26	Recent scars from chancre—10 mos Roseola—4 days		Frequency dysuria	3 papules near neck	Symptoms disappeared after antiluetic treatment No control	
147	Colodero and DiLella 1st case	1930 M 44	No venereal history Left vesicle enlarged and tender	Negative	Hematuria frequency, dysuria, 1 mo	Vegetating lesions and ulcers on trigone and lateral wall	After 6 neoarsphenamine—no symptoms and control—all lesions practically disappeared	
148	2d case	1930 M 52	Gonorrhea at 16 years Chancre untreated X ray negative Large prostate	Negative	Frequency dysuria	Retention Large prostate Infiltrated mamillated area with cystitis	After 2 neoarsphenamine—no symptoms and control—normal bladder After 6 neoarsphenamine and 10 mesurol negative	
149	Chocholka 1st case	1931 F 45	3 abortions. Bacteriology negative	Negative	Frequency, dysuria 3 yrs	Grayish white membrane over trigone	Local treatment failed 2 mos after potassium iodide no symptoms and control—disappearance of most of leucoplacic membrane	
150	2d case	1931 F 36	1 abortions Specific ulcer at urethral meatus Urethral stricture			Ulcer, edema and scars about neck of bladder with circinate cicatrices at right ureter	No control	No gonococci or tubercle bacilli

TABULATION OF CASES—Continued

Case	Author	Year Sex Age	History of syphilis or concomitant lesions	Wassermann	Genito-urinary symptoms—duration	Cystoscopic or operative findings	Results of specific treatment and cystoscopic control	Incidental bacteriology, histopathology or other laboratory findings
21	[illegible] case	[illegible]	Treated for lues [illegible] years ago. Hypertrophy of prostate	Positive	Frequency, dysuria	Ulceration and cicatrices all over bladder	Antiluetic treatment difficult because of cardiac complications. No control	
	[illegible] case	[illegible]	No luetic history. Gross-data lues condition of [illegible] and right testicle [illegible] yrs.	Negative	Frequency, dysuria, Fever [illegible]	Pseudo-membranous with ulceration	After [illegible] treatment left wall and urine clear. After no treatment complete cure and control—normal bladder [illegible] yr later cystoscopy showed sclerosis, no tubercle bacilli	No gonococci or tubercle bacilli
23	[illegible] case	[illegible]	Right kidney movable, large and tender. Recovering from [illegible] for gummata of liver		Frequency dysuria	Tuberculosis and edema. Catheter specimens from both sections—white blood cells and albumen		
24	[illegible] case	[illegible]	Lues [illegible] yrs ago. No gonorrhea. Acrodynia		Hematuria, frequency dysuria, Fever [illegible]	Papillomata. Dense from right kidney, pus, no gonococci, no tubercle bacilli. Urine from left kidney sterile	Antiluetic treatment recommended. No control	
	[illegible]	[illegible]	No venereal history. Pertussis. Genital tract lesions [illegible] and negative. Wassermann. Prostatic sclerosis	Negative	Frequency dysuria, [illegible] yrs	Villous papillomatous growth of trigone. Cystitis—contracted bladder with irregular edges	[illegible] days after nonspecific urethritis lesions disappeared only slight cicatrices remaining. Later urine cleared, and prostatic became normal	Bacillus coli and streptococci in culture
26	Tuberculosis case	[illegible]	Chancre [illegible] yrs ago with specific treatment. Wassermann negative. After antiluetic treatment normal persists	Positive	Frequency dysuria, [illegible] yrs	Syphilomata of left wall and left ureteral orifice	[illegible] after antiluetic treatment syphilomata disappeared. Only slight edema remained. [illegible] after antiluetic treatment control—normal bladder	Hyperplasia of endothelial cells with [illegible] with mononuclear cells of chronic inflammation, lymphocytes and plasma cells. Cystic cavity in center with degenerating cells. Part homogeneous showing no structure and no evidence of necrosis
27	[illegible] case	[illegible]	Gonorrhea at [illegible] yrs with slight morning gleet [illegible] yrs. Hematuria for few days [illegible] ago	Positive	Hematuria	Vegetating syphilomata	[illegible] days after antiluetic treatment hematuria ceased and dysuria improved. After [illegible] operation and [illegible] months control—normal bladder [illegible] weeks after 1st cystoscopy	Chronic inflammation with hyperplasia of epithelium [illegible] sections shows hyperplasia of epithelium [illegible] tendency to [illegible]. In the chancre there is [illegible] fibrosis with the cells of chronic inflammation
28	Levy and Tripoli	[illegible]	[illegible] of symptoms prior to operation for tuberculous cyst, causing abdominal pain, but no urinary symptoms	Positive	None	Operation revealed flat tumor ([illegible] cm [illegible]) overlying bladder. In freeing mass the bladder was accidentally opened. Mass was adherent to left. All of mass and contained necrotic material resembling [illegible] Adjacent bladder wall—hard and friable. Bladder closed and drained suprabubic. Suppurative fistula developed	Cystoscopy after operation revealed the bladder tract. In spite of antiluetic treatment, the patient died and autopsy revealed peritonitis and numerous [illegible] plaques diffusely distributed over bladder with tumor mass in right upper corner of bladder showing central necrosis	Specimens at autopsy showed endarteritis with thrombosis and perivascular lymphocytic infiltrations, occasional [illegible] endothelial plaque cells and small areas of necrosis

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RUPTURE OF THE GRAAFIAN FOLLICLE AND CORPUS LUTEUM

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RUPTURE of the graafian follicle or corpus luteum of the ovary, whether physiological or pathological, may cause symptoms of severe or mild abdominal pain, may be serious enough to require immediate operation or may be so inconsequential that observation and rest in bed is the only treatment necessary. Certainly in many cases of "appendicitis" in young women operations have been done with a mistaken diagnosis. A more thorough knowledge of the symptoms and physical findings of this condition is important for all surgeons and gynecologists.

HISTORICAL

This entity is not a new one, but a large series of cases from one clinic is unusual. Ravdin found that Nélaton in 1851 was aware of the possibility of hemorrhage from a ruptured graafian follicle. H. W. Wilson in 1905 first reported finding a ruptured ovary at operation. In 1914 von Beust reported 36 cases which he had collected from the literature, and in 1917 Novak brought this number up to 40. In 1922 Moore added 14 cases. In 1924, Phaneuf analyzed the reported cases and found 42 cases of rupture of either the graafian follicle or the corpus luteum. In 1926 Brakeley and Farr added 14 more cases. R. K. Wilson in 1928 supplied 7 additional cases. V. E. Johnson reviewed the literature in 1930 and found the total reported cases to be 77. Miller added 4 of his own in 1931. Boggon and Wrigley added 13, and Sackett added 16 cases of his own in 1932. Morton found the total number of cases reported through 1931 was 95. In 1933, we reported 25 cases from the Massachusetts General Hospital.

MATERIAL

In the years 1929 to 1934, inclusive, there have been in the Massachusetts General Hospital 58 patients who have had hemorrhage from rupture of the graafian follicle or corpus luteum that has caused symptoms severe enough to require operation. Such a series of cases brings attention to a problem of major proportions. The house officers and resident surgeons in the emergency ward have been looking for this condition in young women with abdominal pain. Consequently an accurate diagnosis has been made before operation in 17 of the 58 cases; this is an unusual experience.

SYMPTOMS

Patients following rupture complain of sudden pain which is usually in the right lower quadrant. They may or may not have nausea and vomiting. In some instances the pain is extremely severe and the patient is greatly prostrated. This is most usual in those patients with large hemorrhages. Faintness occurs in the severe type. Pain at the top of the shoulder, which is noticed by some, is due to blood reaching the diaphragm, the pain being referred through the phrenic nerve.

ANALYSIS OF CASES

Of the 58 cases in this series, the ages of the patients range from 14 to 41. Thirty were between the ages of 15 and 20 years, and 14 between 21 and 25. Forty-eight were single and 10 were married.

Thirty-nine patients complained of a sudden sharp pain at the onset, 17 of a gradual onset, and 2 did not state the manner of onset of the pain. Forty-eight located the discomfort in the right lower quadrant. One had generalized abdominal pain finally localizing in the right lower quadrant. Another patient had left upper quadrant pain eventually localizing in the right side. In 1 case each, the pain was located in the lower abdomen, the right groin, and in the midline of the abdomen. One patient complained of having abdominal cramps.

Nausea was present in 22 cases, slight nausea in 13, and no nausea in 23 cases. Twenty-four patients had vomited while 34 did not.

Fainting at the onset occurred in those cases with severe hemorrhage as did pain at the top of the shoulder. Previous attacks had been experienced once by 8 patients, several attacks by 10 patients, and occasional discomfort by 1. Twenty-six patients had never had a similar attack, while in 3 cases it was not stated. Only 1 patient had had a previous surgical operation which was for a ruptured ectopic pregnancy. The 57 others had never had a previous abdominal operation.

The previous menstrual cycle had been normal in 47 patients, irregular in 5, and was not mentioned in 6. One patient had a normal pregnancy 11 weeks previously and had not menstruated since the pregnancy. One had amenorrhea for 1 year and 1 month previous to her ruptured follicle. Considering the menstrual cycle as beginning

with the first day of menstruation, the rupture occurred on the following days of the cycle

7th day	3
10th day	1
11th day	1
14th day	24
16th day	1
18th day	3
19th day	1
21st day	9
24th day	1
25th day	3
At onset	2
Not stated	9

PHYSICAL EXAMINATION

The physical signs, usually slight in the mild cases, were more severe if there was considerable hemorrhage

Most of the patients were tender in the right lower quadrant but only a few had real spasm The tenderness occasionally extended across the abdomen near the symphysis to Poupart's ligament and varied greatly with the amount of blood in the abdomen, those with a large amount of blood being exquisitely tender Tenderness by pelvic or rectal examination was present in patients with blood in the pelvis Motion of the cervix caused pain only when a considerable amount of fluid or blood was found

The rectal temperature averaged 99 5 degrees but ran as high as 102 degrees The pulse averaged 98 beats per minute, the highest being 130 Urinalysis was negative in all cases The white blood count varied from 5,000 to 27,000, but was not done in 11 cases

White blood count	Cases
5,000 to 10,000	22
10,000 to 12,000	9
13,000 to 14,000	8
15,000 to 17,000	2
19,000 to 20,000	3
21,000	1
24,000	2
27,000	1

The white blood count was normal or not higher than 10,000 to 12,000 in the mild cases Patients with a large amount of blood in the abdomen had white counts which were more elevated

DIAGNOSIS

The accurate diagnosis is difficult but can be made In any differential diagnosis the possibility of such a lesion should always be considered Not surprisingly, most of the mistakes were made in confusing the rupture with appendicitis The pain and right lower quadrant tenderness are especially confusing In the severe cases extrauterine pregnancy must be differentiated To rule out such ectopic gestation is very difficult and there is no true differential point Experience has taught us that even at operation such mistakes are not infrequent Careful consideration must be given to the ovary to avoid calling a ruptured ovary an ectopic pregnancy

The status of the menstrual period is of importance, for when the rupture occurs in the mid intermenstrual time it usually means a ruptured follicle and, when it occurs from the fourteenth day to the onset of the catamenia, it indicates bleeding from the corpus luteum To make the diagnosis, a careful history concerning the onset of the pain, its suddenness and severity is essential The presence of fainting and shoulder pain are very important A careful menstrual history, especially noting the *beginning* of the last period, and the presence of previous similar attacks is also important The pulse varies according to the amount of blood lost and the temperature with the time since the onset of the rupture

The pre-operative diagnoses in this series were as follows

Appendicitis	33
Ectopic pregnancy	2
Salpingitis	4
Tuberculous salpingitis	1
Ruptured graafian follicle	3
Ruptured corpus luteum	14
Undiagnosed	1

At operation ruptures of the ovary of the following types were found

Ruptured graafian follicle	10
Ruptured corpus luteum	45
Ruptured corpus luteum cyst	1
Follicle or corpus luteum (ruptured) ?	2

Hemorrhage from the corpus luteum is much more frequent than from the graafian follicle One patient also had an acute appendix, but here the diagnosis of appendicitis and ruptured corpus luteum were both accurately made

TREATMENT

The authors believe that nearly every female patient who is operated upon for appendicitis should have a lower abdominal paramedian or midline incision Through either incision the pelvis and ovaries can be explored under direct vision Often the amount of blood or fluid from the rupture does not rise above the pelvic brim and, in several of the cases of rupture of the graafian follicles, thick clear coagulum has been found in the pelvis, which would be difficult to find through the ordinary incision for appendicitis

When the abdomen is opened either blood or bloody fluid may be easily detected Sometimes it is necessary to explore the pelvis carefully in order to find a moderate amount of the coagulated material, and the ovary may show a recent opening without bleeding If the rupture occurs so that a vein is torn, hemorrhage may ensue immediately If the small hematoma, which normally forms in the ruptured follicle and represents the early stage of the corpus luteum suddenly ruptures, hemorrhage occurs. This may take place any time from the rupture of the follicle to the onset of the next menstruation.

In our series the type of fluid present in the pelvis and abdomen was as follows

Red blood	29
Blood stained fluid	15
Yellow fluid	4
Old blood	
Not stated	8

Every effort should be made to conserve the ovary In those who are actively bleeding the opening can be closed or the lining of the lesion can be shelled out and the defect closed with a fine atraumatic suture. A rubber covered gastric clamp lightly placed on the ovarian blood supply controls the hemorrhage while the ruptured area is being sutured.

The treatment of the ovary in this group was as follows

	Cases
Nothing done	37
Mattress suture	7
Oophorectomy	11
Cyst removed	6
Both ovaries removed	1
Hysterectomy and oophorectomy	1

The right side was involved 39 times and the left 13 times and in 6 cases it was not stated. The appendix was removed in all cases except those with profuse hemorrhage and the pathological report of the removed appendix was negative in all but the acute case mentioned.

In retrospect many of these mild cases need not have been operated upon The danger in not operating lies in the close resemblance the symptoms bear to those of acute appendicitis. In the cases of severe hemorrhage operation must be done

IMPORTANCE OF DIFFERENTIAL DIAGNOSIS

According to most recent investigators, the time of rupture of the graafian follicle is at the mid point of the intermenstrual period. That is, the egg is released from the follicle on the twelfth to the fifteenth day following the onset of menstruation or to put it another way from the twelfth to the nineteenth day before the oncoming period —(Ogino, Knaus, Shaw Miller) It is at this time that pain may occur and some women, on careful history taking will recall instances of such discomfort. Usually there is no pain enough discomfort may be present, however to decide the patient to visit a surgeon. Bleeding may conceivably occur from small veins about the follicle if the rupture is at all abnormal. At this time *clear white to yellow coagulated material will be* found in the pelvis, and if bleeding has occurred, a moderate amount of blood After the follicle has ruptured a blood clot forms in the ovary and the corpus luteum is in the process of forming From such a body bleeding may easily occur and may be severe if the clot is loosened or mild if the bleeding comes from a small ruptured vein or its surface. The differential diagnosis between follicle and corpus luteum is not difficult and the operative findings usually decide which is responsible. Discomfort in any woman from the supposed time of ovulation to the oncoming menses may be due to rupture or bleeding.

The cause of the rupture is not clear but trauma has often been mentioned as a cause. We have not been able definitely to trace the cause to trauma in any of our cases. Cases have been reported by Christopher Greeley and others and most surgeons have been conscious of rupturing a small physiological cyst at one time or another Trauma is conceivable as an etiological factor but a slightly abnormal ovulation or abnormal blood clot formation seems easier to consider the important factor

It is necessary to realize that such happenings are possible and it behooves us all to be on guard against a lesion suggesting appendicitis that may not need operation at all or that may need urgent surgery because of hemorrhage.

SUMMARY

1 Fifty-eight cases of rupture of the graafian follicle or the corpus luteum simulating other acute abdominal disease are reported

2 Trauma has not been found to be an etiological factor in any case in this series.

3 The relation of the onset of symptoms to the day of the onset of menstruation is an important diagnostic point

4 The sudden onset of pain, low temperature, slightly elevated pulse, and low white blood count, all out of proportion to the pain, are suggestive of this lesion in the mild cases.

5 Patients with severe hemorrhage following rupture show signs of a more diffuse tenderness,

are sometimes faint, and have referred phrenic nerve shoulder pain

6 A lower abdominal paramedian or midline incision is advised, so that the ovaries may be explored under direct vision

7 The ovary should be conserved if possible The lining of the lesion may be shelled out and the ovary reconstructed with a fine atraumatic suture

8 This normal or pathological physiology of the ovary should be considered in the differential diagnosis of acute abdominal pain

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EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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JANUARY 1936

ACID ULCER

THE extensive literature and numerous current papers on all phases of gastric and duodenal ulcer testify both to the importance of the problem and to the prevailing uncertainty with respect to etiology and treatment Indeed many writers go so far as to say that the cause of ulcer is entirely unknown a stand which is hardly justified in view of the many facts which have been uncovered in various laboratories in the past few years As a direct result of planned experimental procedures the disease has been caused to develop in the lower animal and to duplicate in almost every particular the lesion encountered in man The gross and histological appearance of the experimental ulcer exactly resembles the clinical lesion and it has been observed to perforate to cause profuse hemorrhage and to heal under a type of medical management which resembles that found effective in man In addition the alterations in the physiology of the alimentary tract under which experimental ulcers may be expected to develop and become chronic are well understood and the factors involved may be fairly accurately appraised. It does not lessen the significance of this experimental work to concede that much of the knowledge is not new and that the evidence obtained from the lower animal in large part only substantiates older views that have arisen as a result of clinical experience and reflection

The work of Exalto and of Mann and his associates provided for the first time a method for the regular production of ulcers in the intestines of dogs, without the use of external corrosive agents. Their finding that the diversion of bile and pancreatic juice to the exterior or into the lower ileum would lead to the development of perforating ulcers in that part of the small intestine which first receives the gastric content has been amply confirmed There seems no reason to question the view that it is the neutralizing effect of the alkaline pancreatic juice which normally protects the duodenal mucosa from the acid gastric content It is probable that the clinical application of this finding is not direct since it does not seem likely that bile and pancreatic juice often fail to reach the duodenum. A few such cases have however been observed The chief significance of the work lies in the unequivocal support that it affords to the old theory that the corrosive action of the gastric juice under certain circumstances, may produce and maintain a chronic ulcer

The observations of the writer and his associates that all living tissues will succumb to the digestant action of the gastric juice where conditions are such that they are exposed to the pure undiluted secretion pro-

vides further support to the theory of the "peptic" genesis of ulcer Whereas it was found that organs such as the spleen and kidney, when implanted into the wall of the normal stomach and consequently exposed to the usual gastric content remained little affected, they were promptly digested away when they were implanted into the wall of an isolated stomach pouch and exposed to the action of pure undiluted gastric juice In a somewhat similar type of experiment it was demonstrated that the pure fundus secretion can digest away the normal mucosa of the alimentary tract including that of the stomach itself, the resulting defect displaying all the gross and histological features of chronic progressive ulcer in man Under normal conditions the gastric juice is diluted and partly neutralized by swallowed food and saliva, the secretion of mucus from the pyloric antrum, and to a certain extent by the regurgitation of bile and pancreatic juice Since the fundus secretion appears to be elaborated at a constant acidity it is clearly this neutralization that protects the mucosa from ulceration A failure in this neutralizing mechanism would lead to the development of a progressive ulcer in the stomach or duodenum even though the mucosa was previously normal This fact is of considerable significance since it makes it unnecessary to postulate a local loss of resistance of the mucosa to account for the lesion The careful histological examination of a large number of resected stomachs in Konjetzny's material failed to reveal evidence of local vascular injury, embolism, or thrombosis as called for in the theory of Virchow and Hauser It is not to be supposed, however, that the resistance of the mucosa to digestion would always be uniform throughout or that a uniform exposure of the entire surface would always occur Such variations should be of chief significance in determining the site of the resulting ulcer and its shape The more general effect is manifested by the small erosions, hemorrhages, and cellular infiltrations in the neighboring more resistant or less exposed mucosa According to this view the so called ulcer gastritis is of similar origin to the ulcer itself It should be more amenable to medical treatment and perhaps for this reason is seen less frequently in those cases subjected to prolonged medical management before referred for surgical treatment

A very important remaining problem is to outline those factors which lead to the accumulation in the stomach of a content that resembles pure gastric juice in acid and enzyme concentration Pyloric stenosis with retention and excessive "continuous secretion" are two conditions which come readily to mind Pyloric stenosis may raise the acidity of the gastric content by causing a long continued secretion of gastric juice and possibly also by preventing the backward regurgitation of duodenal secretions as indicated by the studies of Boldyreff and of Elman The mechanism of the "continuous secretion" of gastric juice is little understood and the factors that alter its volume are unknown There is evidence that this secretion is excessive in many ulcer patients, and is perhaps "nervous" rather than "humoral" in origin

Of the two elements, pepsin and hydrochloric acid in gastric juice, it is the concentration of acid that determines the ability of the secretion to digest living tissue When the legs of living frogs were exposed to the digestant action of gastric juice samples of varying acid and enzyme concentrations the extent of digestion was proportional to the concentration of acid and little if at all to the pepsin Approximately 0 15 per cent free hydrochloric acid was the critical level below which the living tissue was not affected When the acidity of the juice exceeded this level

the exposed living tissue was digested away although the pepsin concentration had been reduced to a tenth of its original value It is doubtless significant that the free acidity of the normal gastric contents of man rarely exceeds 0 15 per cent (42 clinical units) and that higher values are commonly found in ulcer patients. The relatively greater importance of the acid in the genesis of ulcer is further suggested by certain observations made with pancreatic juice. The proteolytic enzyme of pancreatic juice trypsin is more active than pepsin but no tryptic' ulcers of the duodenum in the region of the pancreatic ducts have been described Furthermore the legs of living frogs exposed to pure activated pancreatic juice were not digested away as was the case with gastric juice Accordingly if it seems wise to stress the importance of the chemical action of the gastric content in the etiology of ulcer of the stomach and duodenum the term 'acid ulcer' is more accurate than peptic ulcer" and serves to direct attention to the more important element in gastric juice

LESTER R. DRAGSTEDT

BONE TUMORS

GENERAL apathy of the medical profession regarding malignant bone tumors still prevails and is probably due to the exceedingly high mortality This attitude in the past may also be ascribed to the confusion which existed but the Registry of Bone Sarcoma of the American College of Surgeons has done much to clarify this subject A classification has been given that can be comprehended by the average physician and has been the means of saving many limbs and probably a number of lives

The diagnosis of bone tumors, and in fact many bone lesions, should be preceded by a systematic investigation of the clinical history physical examination, biopsy (with gross and microscopic examination) and in many instances the response to irradiation by X ray and radium. There is some difference of opinion regarding biopsy and such an eminent authority as Ewing believes that an incision into a malignant bone tumor increases the danger of metastasis. However a fairly large percentage of five year cures" give a history of repeated local operations. While it is quite true that an accurate diagnosis frequently can be made by experts without biopsy the average well trained surgeon, without special experience is helpless. The safest procedure where the more malignant types are suspected is to prepare for a radical operation and make a frozen section while the patient is on the table if there is evidence of malignancy amputation or excision may be carried out. Only in case of doubt is it advisable to wait for the report from a permanent section. Frozen sections and sections made from needle or punch biopsies are not as dependable as permanent sections made from blocks of tissue removed surgically but when confirming other evidence of malignancy errors in diagnosis are exceedingly rare One of the greatest difficulties which exists today is the paucity of pathologists who are experienced in bone pathology and can render a reliable opinion. Differentiation between tumor bone and bone in the evolutionary process of repair or reacting to the stimulus of inflammation, cannot always be made with ease Distinction between solitary metastatic lesions and those of primary tumors as endothelial myeloma is exceedingly difficult In very malignant tumors observed during the process of bone destruction, osteoclasts, the giant cell of normal bone repair may be found in such great numbers that there may be a close resemblance to a benign giant cell tumor The important practical point whether the tumor is or is not malignant can usually be

determined Differentiation by roentgenogram between endothelial myeloma (Ewing's tumor) and osteogenic sarcoma can usually be made, though not pathognomonic as each may simulate the characteristics of the other Ewing's tumor responds rapidly to irradiation while osteogenic sarcoma does not

All bone tumors are potentially malignant as malignancy, though rare has occurred even in tumors regarded as distinctly benign Whether this originates from the inclusion of embryonic cells or from primary benign tumor cells is of no practical importance For example cases in which the diagnosis of giant cell tumor has been made by eminent authorities have later proved to be definitely malignant However, it is well known that almost 100 per cent of typical giant cell tumors can be cured by conservative measures If the resemblance between rare malignant variants of giant cell tumors and typical giant cell tumors is so close that well trained men are not always able to make the distinction, from a practical point of view, the possibility of malignancy in apparently benign tumors must be considered, even though remote

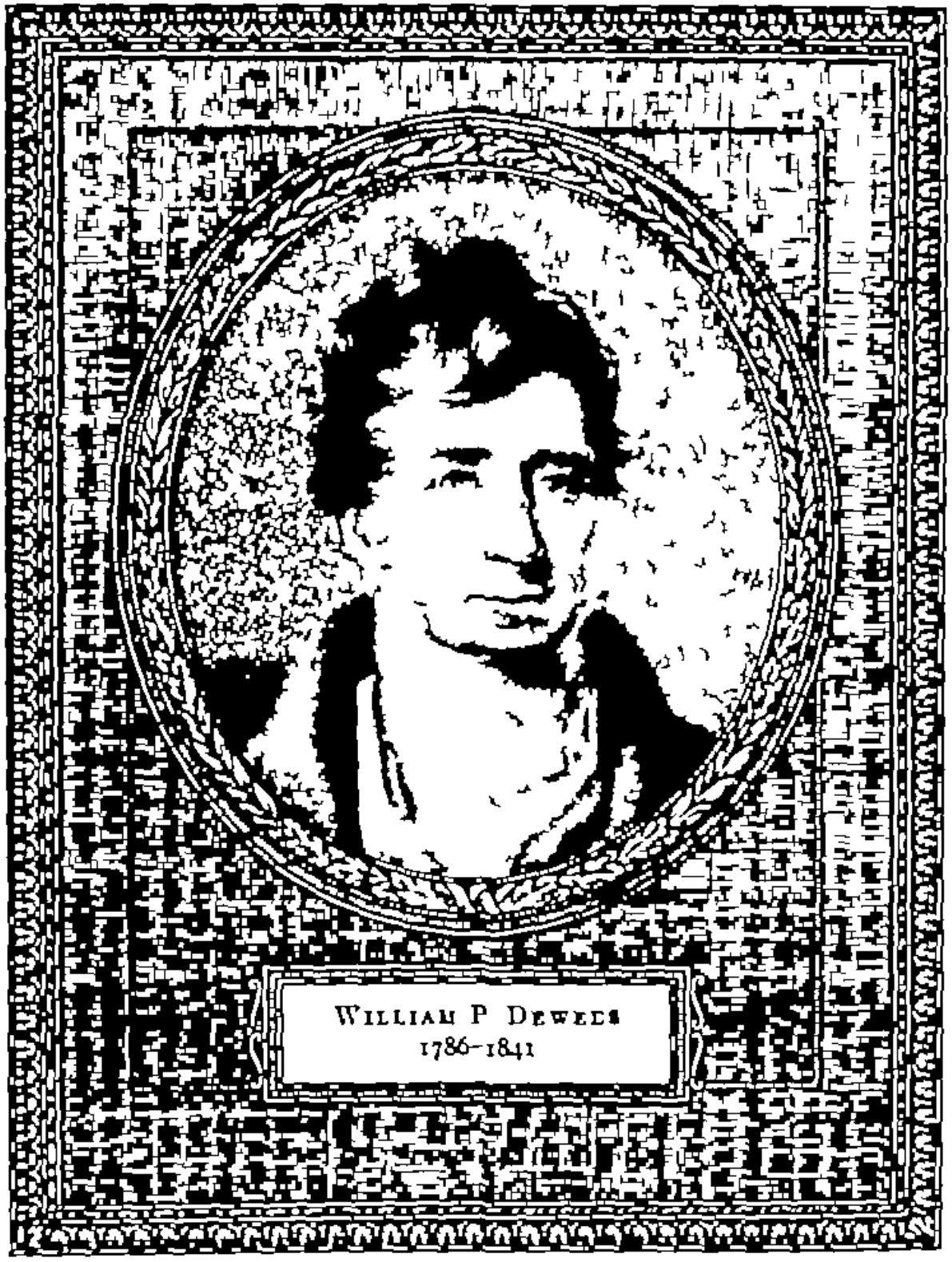
No arbitrary statement can be made as to time in relation to cure Three of the 87 accepted "five year cures" of the Registry of Bone Sarcoma (B S R No 100, No 970 and No 1025) died of metastasis 11, 8, and 13 years, respectively, after treatment However, if two years elapse without evidence of local recurrence or metastasis the chances are good that the five year period will be reached Many of the cases registered as "five year cures" were of low grade malignancy as demonstrated by the history, roentgenogram, and the histology, and even prior to registry, a fair percentage of these were cured by amputation or excision However there are possibly 25 per cent of those registered which were very malignant and are living and well after the elapse of 5, 10 or more years The author has recently reported 14 cases which are living and well after the lapse of 3 to 16 years, 9 of which were malignancies of low degree, and 5 were very malignant This is a vast improvement in results when compared to those of the past and is largely due to the study and advancement stimulated by the Registry I presume the experience of other surgeons has been similar

Secondary malignant changes have been observed in chronic bone lesions such as giant cell tumor mentioned above, osteitis deformans (Paget s disease) osteochondroma chondroma low grade osteitis, etc Some of these can be eradicated before malignant changes have occurred, but if eradication is impossible, by close observation one may detect malignancy in an exceedingly early stage The same attention should be given to premalignant lesions of bone as is given to precancerous lesions such as pigmented moles, scar tissue in the cervix and lump in the breast

Bone is a living tissue and must be so regarded, but the reaction to many pathological processes is exceedingly slow, and a long time may elapse, in some instances one or more years, before abnormal changes are demonstrable by the roentgenogram In very malignant tumors the process is very rapid, and in all probability is demonstrable by the roentgenogram in its incipiency, but very few cases are ever observed before there has been extensive involvement In our experience we have observed only two cases at a very early stage One is living and well after three years and one died as we were unable to make an early diagnosis No one can give an expert opinion in such cases as so few are ever observed in the incipiency The mortality still remains deplorably high, even if the diagnosis is made at a time which we now regard as early But a carefully elicited history will

demonstrate that the diagnosis frequently could have been made weeks or months sooner

The end results in bone tumors, with our present knowledge of treatment, can be improved only by eradicating 'pre-malignant bone lesions as stated above, and by a much earlier diagnosis and treatment of primary malignant tumors than is customary at the present time. It is conceivable that not only may the mortality be decreased but also that less mutilating procedures may be successful. This can be accomplished only by co-operation of the profession and education of the public to the importance of carefully investigating symptoms of pain, with or without tumefaction referable to bone, especially in children and young adults. WILLIS C. CAMPBELL.



WILLIAM P DEWEES
1786–1841

MASTER SURGEONS OF AMERICA

WILLIAM POTTS DEWEES

THE subject of this sketch, William Potts Dewees, was born in Pottsgrove, Pennsylvania, in 1786 His paternal ancestors, the DeWees, were among the original Swedish settlers on the banks of the Delaware Bay and River On the maternal side he was of English descent, his mother being a daughter of Thomas Potts, who was a member of the Society of Friends and for whose family Pottsgrove, or what is now Pottstown, was named

Early in life he determined to study medicine Although his early education was indeed scanty he had learned French and Latin In order better to prepare him for his work his father placed him with a Dr Phyle, a practicing apothecary, where he early obtained a knowledge of both pharmacy and chemistry While still a young man his father died leaving little for his family

After several years with Dr Phyle, during which he showed considerable promise, he came to Philadelphia and apprenticed himself to Dr William Smith He not only assisted Dr Smith but at the same time attended lectures in the University of Pennsylvania from which School he received, in 1789, at the age of 21, the degree of Bachelor of Medicine

Following graduation he moved to Abington, a settlement some miles north of Philadelphia, where he became an active and ambitious practitioner The thoroughness of his work was soon recognized and when in 1793 the yellow fever epidemic had seriously reduced the ranks of the medical profession of Philadelphia, Dewees was induced to move to that city to practice This he did in December, 1793

He entered upon the new field with considerable confidence not only because of the place he had made for himself but because his sponsor was Dr Benjamin Rush Rush was at this time an outstanding figure in American Medicine Phillip Syng Physick and Thomas C James, both of whom had only recently returned from study abroad were his associates and chief competitors Physick, who became the Father of American Surgery, was without doubt an admirer of Dewees, for not long after his debut into Philadelphia he went to Dewees' defense when the latter was maligned by a jealous competitor

The latter part of the nineteenth century found obstetrics in Philadelphia at a low ebb, for as Dr Hodge has so aptly said "at that period the science was

hardly known in America." Midwifery was largely in the hands of nurses and midwives. There was little instruction in it at the medical school. "The physicians who occasionally engaged in its practise had received no instruction with the exception of a few who had brought back a general knowledge of the subject from Europe. The existing prejudices against the employment of a male practitioner for obstetrics provided few opportunities and even fewer inducements for the physician to improve his knowledge in this field. Hence midwifery existed almost universally as an art the aged and imbecile nurse was preferred to the physician

The only training the student in the Philadelphia school could obtain was from Shippen who was already sorely pressed with his practice and his teaching of anatomy and surgery and from Dr Bond who with his already overburdened life had advertised on October 25, 1781 that in connection with his clinical lectures in medicine at the Pennsylvania Hospital he would teach obstetrics

Dewees and Church early realized the opportunities in this field for supplying skillful and intelligent service They began to perfect themselves and to communicate their knowledge and experience to others. Hodge's description of Dewees early efforts is indeed interesting "In a small office he collected a few pupils and in a familiar manner indoctrinated them with the principles of our science toiling year after year in opposition to the prejudices not only of the community but even of the profession who could not perceive that so much effort was necessary for facilitating the natural process of parturition "

In 1806 Dewees was given the degree of Doctor of Medicine by the University His thesis was entitled 'The Means of Moderating or Relieving Pain During Parturition. His work in this field was already bringing real recognition "He has the high honor of first attempting a full course of Lectures on Obstetrics in America It was, therefore, natural that he should be considered a candidate for the new chair of obstetrics but in spite of his qualifications and the warm support of Rush and Physick he failed to be elected and Thomas Chalkley James was elected to the chair in 1810

Under the apprehension of a pulmonary affection he was persuaded by friends to retire from the profession and to invest his capital in a farm near Phillipsburg and here from 1812 to 1817 he lived as a farmer He lost his capital and soon found that his talents lay in the practice of medicine rather than in farming so he returned to Philadelphia after 5 years to attempt to rebuild his practice

In 1825 at the age of 57 he was elected adjunct professor of obstetrics and did much of the teaching of the department He was then described as youthful because of his florid complexion and dark hair which was still "without the silvery gloss of age " He was exceedingly popular as a teacher although there was "no great display of eloquence or erudition in his lectures " He was clear and precise and his directions were given in great detail

patient with nervous and mental disease That such an attempt might serve a useful purpose is at once indicated by the fact that, although nervous and mental derangements are the most common of all disorders, the general practitioner is least acquainted with them, due to the neglect of neurology and psychiatry in the training of the physician The general practitioner who feels that he is handicapped in his understanding of the patient with nervous and mental disease will find this book useful Among the subjects covered are the emotions, migraine, the neuralgias, intracranial tumors, organic reaction types, dyskinesias, disorders of sleep, disorders of the sex life, the neuroses, the psychoses, epilepsy Of necessity, many of the subjects are discussed briefly, sometimes the discussions are no more than extended definitions, but it contains much useful information and surprisingly few misstatements The author's viewpoint throughout is very sane

HARRY A. PASKIND

THE attractive and beautifully illustrated volume[1] by von Lanz and Wachsmuth is a credit both to the industry and thoroughness of its authors, and to the art and skill of the printers and engravers who produced it

Beginning with the upper extremity as a whole the authors consider in turn contour and form, superficial musculature, skeleton and skeletal development, arteries, veins, lymph vessels, nerves, nerve distribution, and the effects of nerve injury Following a general survey each part of the upper extremity is taken in turn shoulder, axilla, arm, elbow, forearm and hand, and the description of each region illustrated by plates, engravings, diagrams and line drawings—many of them in color—and portraying each part from many angles and aspects as well as in cross section

This volume should be a welcome addition to the library of the surgeon who is interested in the surgery of the upper extremity, and of very real help to him as he prepares himself to attack the surgical problems in which it is involved

SUMNER L KOCH

THE present volume, *Chirurgie de la tuberculose pulmonaire*,[2] is an excellent practical treatise on the surgery of pulmonary tuberculosis written by two of its most distinguished exponents The authors have made no attempt to present a complete historical review and in the preface state definitely that the work is an exposition of the methods which they use personally and with which they have had an important experience It has, therefore, the advantages and disadvantages of this limitation While it loses something as a historical summary and a work of reference and bibliography, it gains much as a practical guide The literature has been reviewed and referred to whenever it could throw light on the subject under discussion

The first section considers the various theories which have been advanced to explain the retraction of the tuberculous lung and the principle of selective collapse The extensive text and abundant illustrations describing the anatomy of the thorax and the technique of the operations are sufficient in themselves to make the volume valuable to any one interested in surgery of the chest, and the discussions of problems of surgical procedure are thorough and satisfactory

The indications and results are not well dealt with One cannot go to the book for information concerning the precise rôle of collapse therapy in the treatment of tuberculosis, and there are very few statistics on the results obtained from the different procedures These are important aspects of the subject and while the authors undoubtedly considered that their concern was chiefly with matters of surgical procedure, one feels that chapters on the indications for collapse therapy in general and on its results would add greatly to the value of the work.

But this is to criticize the book for what it does not pretend to be and it is an excellent treatise on the surgery of pulmonary tuberculosis

JEROME R. HEAD

TO make the surgeons of our generation conscious of their indebtedness to Hugh Owen Thomas and to help them appreciate the background of Sir Robert Jones is a worth while undertaking, and we are much indebted to the author of this little volume[3] for making accessible in so interesting a form an account of Thomas' life and of his contributions to surgery In its pages and illustrations there lives again the shy, slender, clear thinking, often irritable recluse who was both one of the earliest and one of the greatest of orthopedic surgeons We see him with closely buttoned frock coat, with ever present cigarette, with cap tilted at a rakish angle over the left eye working in his surgery, correcting club feet, reducing dislocations, tapping and "damming" nonunited fractures, and in the cramped quarters of Liverpool workmen and dock laborers treating compound fractures of the lower extremities, and in all his work achieving results on a par with those obtained today in a modern and well equipped hospital

He did not, moreover, confine his work or his clear thinking to the problems of orthopedic surgery He was interested in many fields of medicine and surgery, he was expert in the use of the lithotrite, he advocated rational methods of treatment of typhoid fever and of intestinal obstruction that are recognized as such today and that are in accord with modern therapeutics He "had a coherent method

[1] PRAKTISCHE ANATOMIE EIN LEHR UND HILFSBUCH DER ANATOMISCHEN GRUNDLAGEN AERZTLICHEN HANDELNS By Dr T von Lanz and Dr W Wachsmuth Vol 1, part 5—Arm Berlin Julius Springer 1935

[2] CHIRURGIE DE LA TUBERCULOSE PULMONAIRE INDICATIONS, TECHNIQUES RÉSULTATS By A Bernou and H Fruchaud Paris C Doin et Cie 1935

[3] HUGH OWEN THOMAS HIS PRINCIPLES AND PRACTICE. By D McCrae Aitken M A. M B Ch.B (Ed) F R.C S (Ed and Eng) London Oxford University Press 1935

of treatment based on the principle of physiological rest for any inflamed tissue," and this principle be applied in a logical manner to all the problems associated with inflammation no matter in what part of the body

The surgeon of today needs to know more of the great heritage of the past, and Albee's volume will help him to realize more keenly the debt of all surgeons and, particularly of orthopedic surgeons to Hugh Owen Thomas

Bernard L. Korn

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender Selections will be made for review in the interests of our readers and as space permits

DISEASES OF THE NOSE AND THROAT, FOR PRACTITIONERS AND STUDENTS By Charles J Imperatori, M D F A C S and Herman J Burman, M D Philadelphia, London and Montreal J B Lippincott Co 1935

THE STOMACH AND DUODENUM By George B Eusterman, M D F A C P and Donald C Balfour, M B, M D (Tor), LL D F A C S, F R A C and Members of the Staff Philadelphia W B Saunders Co 1935

DISEASES OF WOMEN By Harry Sturgeon Crossen, M D F A C S and Robert James Crossen, M D 8th rev ed St Louis The C V Mosby Co 1935

GROWING SUPERIOR CHILDREN By I Newton Kugelmass, M D Ph D, Sc D New York and London D Appleton Century Co 1935

MECHANICS OF NORMAL AND PATHOLOGICAL LOCOMOTION IN MAN By Arthur Steindler, M D, F A C S Springfield, Ill and Baltimore, Md Charles C Thomas, 1935

THE 1935 YEAR BOOK OF RADIOLOGY Diagnosis Edited by Charles A Waters, M D Associate editor Whitmer B Flint, M D Therapeutics edited by Ira I Kaplan, B Sc, M D Chicago The Year Book Publishers, Inc, 1935

MÉDECINE ET CHIRURGIE PRATIQUES Traitement de Pléthore, technique actuelle du traitement prophylactique By B Stragnoff Paris Masson et Cie, 1935

TUMORS OF THE URINARY BLADDER By Edwin Beer M D Baltimore William Wood & Co 1935

CLASSICAL CONTRIBUTIONS TO OBSTETRICS AND GYNECOLOGY By Herbert Thoms, M D With a foreword by Howard A Kelly Springfield, Ill and Baltimore, Md Charles C Thomas, 1935

JOHN WHITRIDGE WILLIAMS ACADEMIC ASPECTS AND BIBLIOGRAPHY By J Morris Slemons Baltimore The Johns Hopkins Press, 1935

SURGERY QUEEN OF THE ARTS, AND OTHER PAPERS AND ADDRESSES By William D Haggard, M D F A C S D C L Philadelphia W B Saunders Co 1935

REGIONAL ANATOMY ADAPTED TO DISSECTION By J C Hayner B S M D Baltimore William Wood & Co 1935

PRESCRIPTION WRITING AND FORMULARY THE ART OF PRESCRIBING By Charles Solomon, M D Philadelphia, London, Montreal J B Lippincott Co 1935

VEIT'S HANDBUCH DER GYNÄKOLOGIE 3d rev ed ed Edited by Dr W Stoeckel Vol 4, and half—KLINIK DER GYNÄKOLOGISCHEN ROENTGENTHERAPIE 2d part—DIE BEHANDLUNG DER BOSARTIGEN GESCHWULSTE By H Wintz and F Witterstaedt Munich J F Bergmann, 1935

ANTENATAL AND POSTNATAL CARE By Francis J Browne M D (Aberd), D Sc F R C S (Edin) F C O G London J & A Churchill, Ltd 1935

LOCALIZED RHEUMATIC CONDITIONS OF BONE AS EXEMPLIFIED BY LEGG PERTHES' DISEASE, OSGOOD-SCHLATTER'S DISEASE, KÖHLER'S DISEASE AND RELATED CONDITIONS By E S J King, M D D Sc M S (Melb) F R C S (Eng) F R A C S Baltimore William Wood & Co 1935

THE PATIENT AND THE WEATHER By William F Petersen, M D Vol Part The Footprint of Asclepius Ann Arbor Mich Edwards Brothers, Inc 1935

LIPPINCOTT'S NURSING MANUALS Principles of Ethics By Dora Thomas Verner Moore Ph D M D Philadelphia, Montreal, and London J B Lippincott Co 1935

DEMONSTRATIONS OF PHYSICAL SIGNS IN CLINICAL SURGERY By Hamilton Bailey F R C S (Eng) 5th rev ed Baltimore William Wood & Co 1935

THE PARATHYROIDS IN HEALTH AND IN DISEASE By David H Shelling, B Sc M D St Louis The C V Mosby Co 1935

ATLAS OF PATHOLOGICAL ANATOMY Issued under the Direction of the Editorial Committee of the British Journal of Surgery Compiled by E K Martin, M S F R C S Vol Baltimore William Wood & Co 1935

THE RADIOLOGY OF BONES AND JOINTS By James Y Bradford, M D (B'ham) M R C S (Eng) 2d ed Baltimore William Wood & Co 1935

THE ROCKEFELLER FOUNDATION International Health Division Annual Report 1934 New York

THE CERVIX UTERI WITH SPECIAL REFERENCE TO THE DEVELOPMENT OF CANCER By R Francis Matters, M D M S, F R C S F F R A C S M C O G D G O Adelaide The Hassell Press, 1935

A MARRIAGE MANUAL, A PRACTICAL GUIDE BOOK TO SEX AND MARRIAGE By Hannah M Stone, M D and Abraham Stone, M D New York Simon and Schuster 1935

SURGERY, GYNECOLOGY AND OBSTETRICS

AN INTERNATIONAL MAGAZINE, PUBLISHED MONTHLY

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THE RELATION OF CHRONIC MASTITIS TO CERTAIN HORMONES OF THE OVARY AND PITUITARY AND TO COINCIDENT GYNECOLOGICAL LESIONS

PART I—THEORETICAL CONSIDERATIONS AND HISTOLOGICAL STUDIES[1]

HOWARD C TAYLOR, JR., M D F.A.C S, NEW YORK, NEW YORK
From the Memorial Hospital

THE relationship between the neoplasms of the breast and the glands of internal secretion has been the subject of study at the Memorial Hospital for a number of years The first paper published in 1929 consisted in a collection of the older literature and an analysis of the clinical evidence of endocrine disease found in the histories and physical examinations of 271 patients with breast neoplasms A second contribution in 1933 recorded further clinical observations in 101 cases of so called chronic mastitis, in particular the effects of treatment by pelvic operations, ovarian therapy, and radiation of the ovaries In the present paper, based on the work of the last 2½ years, report will be made of a series of histological studies and the results of quantitative tests for certain hormones of the ovary and anterior pituitary made upon patients with various forms of generalized breast disease

The diffuse breast conditions, commonly included in the term chronic mastitis, have been the special object of the present study, since these give at once greater indications of a constitutional or endocrinological basis than do the circumscribed tumors The types selected have been three the so called painful breast, certain forms of general hypertrophy, and the breast with abnormal secretion from the nipple

The problem of the etiology of these conditions has been approached in three steps

A Their histology has been reviewed in the light of the histological changes now said to take place in the normal breast in relation to the menstrual cycle For this purpose a new series of 41 sections of breast tissue obtained at known phases of the menstrual month has been collected and compared with histological sections from cases of diffuse breast disease

B A series of 261 cases divided among 183 with painful nodularity of the breasts, 31 with enlargement, and 47 with secretion has been clinically studied by gynecological history and examination and in part by actual observation of the uterus and its appendages at the time of operation for coincident pelvic disease From data so obtained the cases have been classified in 8 groups, giving different degrees or types of endocrine disturbance

C Typical representatives of these groups have been selected for laboratory tests to show blood levels and rates of urinary excretion of estrin and prolan The report on these biological studies and the clinical data noted in B are to be published in a succeeding number of this journal

[1] This work has been aided by a grant from the Egbert C Fuller Fund

Such a study of the relationship between these breast diseases and the perhaps analogous disorders in the female pelvis, with an investigation of the agents which may simultaneously affect or correlate the two areas, should be an important step in the constitutional study of mammary tumors. It has met great difficulties, however in the existing lack of agreement upon the basic pathological process in the disease called chronic mastitis, in the incompletely understood significance of the associated gynecological conditions, and in the technical imperfections of the methods now available for the detection of minor variations in ovarian and anterior pituitary activity

PREVIOUS EVIDENCE FOR AN ENDOCRINE FACTOR IN BREAST NEOPLASMS

In spite of the impression created by the recent outbreak of writing on the endocrinological aspects of breast disease the belief in an ovarian or at least pelvic factor in the etiology of mammary tumors is not of recent origin The theory has indeed developed along three rather definite lines of research, much of which has been recorded in the literature for some years.

A Clinical recognition of a relationship between the pelvic organs and the breast has been built up by the careful observation of outstanding cases in which menstrual abnormalities or anatomical lesions in the pelvis were found in association with various forms of breast disease. Articles on this subject are found scattered throughout the last century and include the writings of Cooper (1829) Velpeau (1854) Witthauer (1902) and Miller (1925) The nature of the agent connecting the two regions was at first a matter of mere surmise, which has given way to a variety of theory with the discovery of the hormones

B Histological study has further developed the conception, for it has been possible to draw comparisons between the morphology of the abnormal hyperplastic processes in the human breast and other conditions in which a hormone cause is more readily provable Examples which may be mentioned are the physiologically hyperplastic breast of pregnancy the mammary glands of animals following treatment by certain hormones, and analogous processes elsewhere in the human body such as the well studied hyperplasia of the endometrium. An important and original contribution of this type was made by Moszkowicz (83-1927) but he has been followed by a number of others (Dietrich Kueckens, Ingleby Borchardt and Jaffé Oliver and Major and Lewis and Geschickter) Each recent worker has shaped his views to fit conceptions, current at the time of his writing of the hormone physiology of the breast.

C Laboratory experiment has led to further important observations. Hypertrophy of the breasts in oophorectomized female animals or in males following the implantation of the ovaries or the injection of estrin was among the first described effects of the ovarian hormone (Steinach Steinach and Dohrn Laquer and co-workers and Laqueur de Jongh and Tausk) That this process may parallel a pathological condition in man has been suggested in the use of the term gynecomastia to describe the hypertrophy in the breast of the male monkey induced by the injection of estrin and anterior pituitary-like hormones (Geschickter Lewis, and Hartman)

Breast conditions said to resemble Reclus disease in their morphology have been produced in mice by Goormagtigh and Amerink by injection of follicular hormone and by Wieser by the use of several hormones alone or in combination, but especially by the corpus luteum Similar effects have been brought about in rats by disturbing the estrus cycle by sterile coitus with vasectomized males (Ingleby) Evans and Simpson (36) have produced adenomas and fibro-adenomas by the continuous injection of anterior hypophyseal extracts, rich in growth hormone, into rats for long periods of time Loeb (1919) and Cori (1927) noted that the incidence of hereditary mammary cancer in mice could be reduced by oophorectomy to a degree varying with the age at which the operation was undertaken Murray has produced mammary cancer in male mice by ovarian implantation after removal of the testes, and Lacassagne by the injection of follicular hormone.

The search of the body fluids of tumor cases as well as the actual neoplastic tissue for

various hormones has resulted in another set of perhaps important, but often conflicting, observations The presence of an anterior pituitary-like hormone in the blood and urine of patients with various genital tumors is now generally accepted An increase of estrin in the urine of cases of granulosa cell tumors of the ovary (Schuschania, Bland and Goldstein), as well as in the blood of many types of malignant growth (Dingemanse, Freud, de Jongh and Laqueur) has also been noted The presence of estrin in the tissue of mouse carcinoma and in certain gastro-intestinal cancers in man has been detected by Silberstein, Fellner, and Engel Of particular interest to this work is the reporting during the last year by Geschickter, Lewis and Hartman of large quantities of estrin in the tissue of a fibroadenoma The principle question of whether these substances are in some way connected with the production of the tumor or are simply the by-products of its cellular activity has received no final answer

HORMONAL INFLUENCES ON THE DEVELOPMENT AND FUNCTION OF BREAST

The development of the breast has for a long time been referred to an ovarian activity and recently more specifically to an ovarian hormone The earliest evidence was afforded by the failure of the breasts to develop in women whose ovaries were removed before puberty and their atrophy after oophorectomy and in the menopause Early castration and ovarian implantation experiments in animals confirmed this relationship (Halban, 52, Knauer) In a later phase breast development was reported following the injection of various organ extracts which have now been shown to have contained the estrus producing or so called follicular hormone With the development of the Allen-Doisy test for the recognition of the estrus hormone, a more definite relationship of breast development to this hormone has been possible and numerous workers have reported not only an enlargement of the gland structure, but of the nipples and areolæ as well, with injection of follicular hormone in a large series of animals, such as rabbits (Vitemberger, Turner and Frank 126), guinea pigs (Laqueur et al, Steinach et al, Champy and Keller, Haterius, 55, Loeb and Kountz), rats (Laqueur et al, Allen et al) and monkeys (Allen, E) In women whose ovaries had previously been removed, Werner and Collier have reported activity in the breasts, characterized by a sensation of fulness and actual enlargement, tingling in the gland tree, and erection of the nipple after injections of theelin A similar report was made by Loeser who, however, had used luteohormone in association with the folliculin The latter observations stand in interesting contrast to the success reported in the treatment of the painful breast by ovarian residue and theelin (Cutler, Leriche, 72, Whitehouse)

That the estrus producing hormone or folliculin causes breast growth appears incontestable Disagreement exists as to the extent of growth which it can produce Laqueur and co-workers believe that in the guinea pig and rat it is possible to attain with the estrus hormone alone growth equal to that of pregnancy Turner and Frank (127), on the other hand, assert that, in male and female castrated rabbits, the daily injection of the estrus hormone will cause a growth of the duct system of these glands equal to that produced during continued estrus but that greatly increased amounts of hormone will not carry the development beyond this stage For further proliferation and formation of lobules characteristic of pregnancy or pseudopregnancy they believe a different agent is necessary Vitemberger and Parkes (95) had also independently noted a limit to the development of the rabbit breast which could be produced by estrin alone As the agent for this further development two additional hormones come into consideration, that of the corpus luteum and the anterior pituitary

The relationship of physiological breast hypertrophy to the corpus luteum has long been accepted due to the striking simultaneous development of corpora lutea and the mammary gland in the pseudopregnant rabbit (Bouin and Ancel, Asdell and Salisbury), and by the development of the breast in association with persistent corpora lutea in several animals (Marshall and Halman, O'Donoghue Hammond and Marshall) These were ana-

tomical studies, however and the mere presence of corpora lutea does not indicate that its specific hormone is responsible for all the changes taking place at the moment.

Full mammary development in rabbits was brought about by Parkes (94) by the injection of alkaline extracts of anterior pituitary which he assumed was due to the resulting prolongation of the luteal activity Turner and Frank (127) also described an increased development over the stage produced by follicular hormone alone when corpus luteum extract was added. Corner however reported no proliferation beyond the puberty condition in spayed rabbits following the injection of corpus luteum (progestin) and suggested that Parkes (94) results were due to a direct effect of the anterior pituitary on the breast. Nelson and Smelser have recently shown that lactation may be induced in the absence of any luteal influence in guinea pigs. Evans and Simpson (35) in injecting anterior pituitary into infantile animals noted mammary development before corpora lutea appeared in the ovaries. The exact rôle of the corpus luteum in mammary growth and lactation remains therefore an undetermined question

The relationship of the anterior pituitary hormone to growth, as opposed to function of the mammary gland is difficult to define owing to the problem of determining what part of the glandular enlargement is due to cellular multiplication and what part to swelling of the cells with retained secretion Corner refers to definite proliferation of the mammary gland in spayed virgin rabbits following 2 weeks administration of extracts of whole sheep s hypophysis Evans and Simpson (36) obtained hyperplasia of the mammary glands in *infantile and adult rats by injection of anterior pituitary* but this was possibly effective by way of the ovary Other observers working on the stimulus to lactation refer in general terms to the development of the mammary gland under the influence of the anterior pituitary

The function of lactation has been recognized as something distinct from mere development or growth and due to some separate stimulus. Certain workers have, indeed, observed the appearance of milk after continued injection of follicular hormone alone (Steinach et al, Laqueur et al) but this appears usually to be but slight in amount, perhaps corresponding to the colostrum in the human breast prior to parturition. Turner and Frank (127) suggest that such secretion may arise from the terminal ducts and not be an indication of full alveolar development.

According to Halban s (53) celebrated theory arrived at from a clever analysis of well known clinically observed facts, the breast development in the pregnant woman is due to a substance from the placenta and lactation is really the beginning of involution and due to a cessation of the previous stimulation. Some laboratory confirmation of this view has been given by de Jongh and Laqueur who were able to produce and prolong artificial lactation in adult male and female guinea pigs by giving first large doses of menformon (estrin) and then suddenly reducing the amount Conversely it may be shown that the administration of follicular hormone when lactation is once established may reduce milk secretion in mice (Parkes and Bellerby de Jongh) and rabbits (Smith and Smith) These experiments correspond with the observable diminution in milk supply in lactating women at the onset of a menstrual period or with a new pregnancy

That the anterior pituitary is an active agent in the stimulation of milk production has been demonstrated by numerous workers. The first of these were Stricker and Gruter who injected an aqueous extract of bovine anterior pituitary into rabbits under various conditions and obtained milk secretion. Similar results have been reported by Corner Nelson and Pfiffner Nelson and Smelser and Turner and Gardner There is, however more or less general agreement that partial development of the mammary gland either through the animal s own ovaries as it matures, by implantation of ovaries or by injection of follicular hormone is necessary before the anterior pituitary hormone can be effective. That the hypophyseal hormone is necessary to maintain milk secretion, once the latter is established is shown by experiments on hypophysectomized animals (Allan, H and Wiles, P., and Collip, Selye and Thomson)

The probability exists finally that a specific hormone is present in the anterior pituitary which causes milk secretion Corner found the breast stimulating hormone much less stable than the gonad stimulating hormone Gardner and Turner suggest its closer relationship with the growth promoting hormone because of its presence in alkaline extracts and propose the term galactin Riddle and his co-workers have named a specific lactation hormone (prolactin) for which a special test object is used and which is alleged to be effective clinically in the increase of milk in parturient women (Kurzrok et al) The production of lactation in monkeys by means of galactin and prolactin and the absence of histological changes elsewhere in the reproductive tract after the injection of these hormones has recently been reported (Allen, Gardner, and Riddle)

Summary of the hormone effects on the breast The follicular hormone is the primary agent producing growth of the mammary gland Its effectiveness may be limited to a development of the duct system only In large amounts it may alone cause the production of a little milk in some animal species Its sudden withdrawal apparently results also in some milk secretion either as a direct effect or through a release of pituitary activity A sudden increase in folliculin during active lactation may reduce the milk supply either by substituting growth for function in the breast or by depressing the pituitary The corpus luteum has an undetermined influence on the human breast, although in certain species it apparently carries forward the degree of development attained by the stimulus of the follicle hormone for the formation of lobules and acini The anterior pituitary, possibly by means of a specific lactogenic hormone, appears undoubtedly to further the formation of the active glandular parts of the breast and to produce and maintain the function of lactation

NERVOUS INFLUENCES AFFECTING THE BREAST

The rapid advance made in the knowledge of the functions of the endocrine glands has left in the background the nervous factors which affect the breast This is, however, of considerable importance in the present study on account of the nervous aspects of the painful type of chronic mastitis referred to frequently in the literature and discussed by me at some length in a previous paper

Certain evidence, it is true, exists to indicate a relative independence of the breast from the nervous system Complete severance from its nerve supply by transplantation does not prevent the breast's reaction to the sex hormones or the secretion of milk (Ribbert, Stricker, Grauer and Robinson) Lactation has been found to be unaffected by removal of almost the entire spinal cord in dogs (Goltz and Ewald) and affected only under certain circumstances by removal of parts of the sympathetic (Cannon and Bright, Bacq, Basch)

More recent experiments and observations suggest, however, at least a slight effect of the sympathetic nervous system on the trophic condition of the breast Cannon and Bright in spite of earlier negative experiments, noted that, when a long period intervened between sympathectomy and parturition, the milk supply was markedly reduced The studies of Ernst (34) give more striking implications He found that in dogs with a resection of the sympathetic chain from the stellate downward to the fifth thoracic ganglion, combined with division of the intercostal nerves which contain autonomic fibers, the affected breast showed signs of retrogression, including disappearance of gland lobules, collapse of alveoli, the growth of connective tissue, and the appearance of histogenic wandering cells Ernst (34) described also the atrophy of one breast of a girl who had been operated upon for a ganglioneuroma of the thoracic sympathetic of the corresponding side This patient noted the cyclical premenstrual sensation only in her normal breast, whereas several women having diminished skin sensibility following section of the cutaneous nerves incidental to extensive operations for empyema noted no change in the premenstrual pain An intrathoracic nerve injury, presumably of the sympathetic, has also been suggested as the cause of the unilateral breast atrophy observed in a large percentage of a series of

cases of predominantly unilateral pulmonary tuberculosis (Kokalj-Kowalewska)

The obvious effect of suckling on the continuation of all normal lactation can scarcely be explained except by a mechanism in which a nervous factor plays an important part. It has not been known however whether the discontinuance of nursing caused involution by the pressure of the secretion in the ducts or the absence of nipple stimulation. This question Selye, Collip and Thomson appear to have decided for they found that with the nipple tied but suckling continuing, in spite of the complete stasis of secretion rapid involution did not occur Furthermore, the nervous stimulus of suckling at the nipples of certain glands maintained active secretion in neighboring glands not being suckled. These workers suggest that the act of suckling reflexly stimulates the hypophysis to secrete prolactin, which presumably stimulates the breast to secrete milk

The effect of stimulation of the nipple even on the non-puerperal breast is shown in the grotesque instances cited in the literature of lactation in children (Baudelocque) old women (Murat and Pathisier Bartels) and in males. Samuel has reported 5 cases of secretion including 1 with lumps and 1 with pronounced breast pain following sexual practices involving nipple irritation. One must accept, therefore, the possibility of parenchymatous mammary changes as a result of local stimulation traveling by nervous pathways More remote nervous stimuli having a psychic or central nervous system origin appear also to affect the breast The occurrence of the painful breast in excitable women and the sudden appearance of breast symptoms during periods of emotional tension has been frequently referred to (Lit. Taylor 123) An hysterical basis for secretion from the nipple has also been claimed (Glorieux) A nerve lesion is clearly suggested in the reported mammary crises of tabes in which there is breast secretion and sometimes pain (Thomas and Kudelski Preuss and Jacoby Biberstein Halban 53 Sliding Schmidtpott) and in the cases of nipple secretion with syringomyelia (Roussy and Mosinger Thomas) Lesions of the midbrain have also been cited as the cause of non-puerperal secretion after encephalitis (Riese) and perhaps in association with pituitary tumors (Krestin)

From the observations made by previous writers as well as from the clinical material to be submitted in this report, the possibility of an effect upon the breast of certain disease processes in the pelvis by way of a nervous pathway becomes important. Sympathetic ganglia in the cervix have been frequently described both in man and the lower animals (Frankenhaeuser Jastreboff Blotevogel, 14 Rein Pissemski) A close relationship between these cells and the hormones of the ovary exists, for it has been shown that the cervical ganglion cells suffer degenerative changes when the animal is castrated or its ovaries radiated and that there is regeneration when such castrated animals are treated by ovarian extracts (Blotevogel 15 16 17 Kennedy)

The effect of stimulation of the pelvic sympathetic has been studied to some extent. Stimulation of the cervix in rodents produces lengthening of the estrus cycle with profound effects on the ovary and mammary glands In rats this response to mechanical and electrical stimulation can be abolished by lower abdominal sympathectomy (Haterius, 56, Vogt) The suggestion has been made therefore that the condition of pseudopregnancy with its incidental mammary hypertrophy is initiated by the hormone of the pituitary only after it has itself been activated by stimuli traversing the sympathetic chains from an irritated cervix Evidence of a pelvic nervous factor in the control of lactation itself is found in the experiments of Selye, Collip, and Thomson in which the lactation regularly occurring after cesarean section in late pregnancy was prevented by distention of the uterus with paraffin following removal of the fetuses.

CHRONIC MASTITIS AND "CHRONIC PARAMETRITIS

Histological changes in the cells of the pelvic sympathetic have been described in a condition which the French writers term "pelvic congestion" the Germans "chronic parametritis Brief reference to these condi-

tions among the pelvic lesions associated with the painful breast was made in a previous paper (Taylor, 123) Subsequent search of the literature on chronic parametritis revealed that W A Freund in his classical paper on this subject had written at length on the accompanying nervous symptoms and had emphasized the frequency of nodules and pains in the breast These quite independent observations of the association of a painful process in the breast and pelvis, made as the result of studies having quite different starting points, appear important Furthermore, many of the clinical and pathological characteristics of parametritis or pelvic congestion suggest a similarity to certain forms of chronic mastitis

Chronic parametritis is according to many writers divisible into two phases, a preliminary congestive phase in which intermittent engorgement of the pelvic vessels is present and a later atrophic stage characterized by fibrosis of the fasciæ and aponeuroses of the pelvis and replacement of the muscular fibers of the uterosacral ligaments and the bases of the broad ligaments In the early stages the uterus may be enlarged, the cervix hyperemic and secreting excessively, the ovaries congested and possibly edematous Later with the fibrosis taking the place of congestion, the fundus and cervix are smaller and firmer, the ovaries furrowed, shrunken, and sclerotic, and the uterosacral ligaments shortened The most characteristic physical signs are the tenderness in the supports of the uterus and the rigidity of the uterosacral ligaments Microscopic examination of the paracervical ganglia of Frankenhaeuser may show a perineuritis, displacement of the nerve cells and fibers with connective tissue, and a shrinkage and loss of polygonal shape of the ganglion cells (Freund, W A, Freund, H W, Cotte and Dechaumé)

The symptoms in the congestive stage of the disease consist in diffuse lower abdominal pain, backache and leucorrhea these complaints all being increased before the menstrual periods At first menstruation may be normal or increased, but later there is a steadily decreasing flow till the periods last but 2 days or less (Freund, W A) Nervous manifestations, particularly in the form of anxiety and sexual disturbances are extremely common

Chronic parametritis and pelvic congestion have been referred to a multitude of causes and probably several factors are contributory The following have been mentioned particularly uterine malpositions (Cotte), sclerocysticovaries (Siredey), endocervicitis (Graefe) adnexal inflammatory disease, constipation (Schultze, Freund, W A, Mueller, Opitz Fraenkel), fatigue and certain occupations (Cotte, Siredey), certain sexual difficulties including excessive coitus, certain contraceptive measures, and masturbation (Kehrer, Fraenkel, Freund, W A, Cotte), certain psychosexual disturbances and anxiety states (Kehrer, Fraenkel, Meyer-Ruegg)

POSSIBLE CAUSES OF CHRONIC MASTITIS

1. From a theoretical standpoint a generalized hypertrophy of the breast or a proliferation of certain of its constituents, particularly the ducts and acini, might result from the excessive or prolonged stimulation of the follicle hormone, by a direct or indirect effect of the anterior pituitary or possibly by the corpus luteum Similarly, abnormal secretion might result from stimulation by the anterior pituitary or from a sudden withdrawal of the follicular hormone The histology resulting from such stimulation should at first be a fairly regular epithelial proliferation which might give rise subsequently to various atypical effects after repeated intermittent stimulation and incomplete regression

2 A mechanism similar to that producing chronic parametritis is also a possible factor in the causation of chronic mastitis For such a theory one must assume a nervous effect upon the breast originating directly in some psychic disturbance or indirectly from an irritated pelvic sympathetic system and resulting primarily in vascular dilatation and hyperemia Unfavorable mechanical conditions found in the shape and support of the breast would undoubtedly be contributory A condition of chronic engorgement may lead to secretory disturbances in the breast epithelium, fibrosis, and later perhaps irregular epithelial proliferation The analogy

which can be drawn between the histology of many cases of chronic mastitis and that described for chronic parametritis as well as the frequency with which the pelvic and breast conditions are found together make it necessary to work with such an hypothesis.

THE HISTOLOGY OF THE BREAST IN RELATION TO THE MENSTRUAL CYCLE

The ovarian theory of origin of chronic mastitis rests in part on the alleged existence of a monthly cycle of epithelial proliferation and regression in the breast. On this subject divergent opinions are held by the various German writers although only one study that claiming the most extreme degree of epithelial hyperplasia, is frequently cited in America.

Rosenburg in 1922 studying breast tissue obtained at autopsy and correlated with the menstrual cycle by examination of the ovary and endometrium concluded that there is a sprouting of the duct epithelium to form acini before each menstrual period and an almost complete disappearance of all epithelial structures except the ducts in the intermenstruum. These findings have been accepted with numerous reservations by a considerable group of writers most of whom, however examined only a few cases (Polano Ernst, 33 Sebening Berberich and Jaffé Loeschke Graf and Luchsinger, Centeno) In America the doctrine of a cycle of epithelial growth in the breast has been taken up with enthusiasm Ingleby writes that the premenstrual proliferation is much more rapid than carcinomatous growth Lewis and Geschickter offer a further elaboration in stating that the expansion of the duct system begins at the mid period of the cycle while the increase in acinar elements is to be noted from the twenty-sixth to the twenty-eighth day

Dieckmann reviewed Rosenburg's work and noted that his cases representing the intermenstrual disappearance of the glands were for the most part taken from young women those showing premenstrual proliferation from older ones, in which age and not the cycle might have increased the amount of glandular tissue Dieckmann himself did not find definite evidence of epithelial proliferation and regression but regarded the premenstrual change as a kind of intralobular edema with a loosening of the fibers of the mantle tissue about the acini which was followed after menstruation by a sclerosis of this intralobular connective tissue. With this view Kueckens Dietrich and Frangenheim and Moszkowicz (82) are in substantial agreement and even Ernst (33) and Rosenburg noted certain changes in the connective tissue and in the definition of the lobules as well as their described epithelial modifications. Besides these changes there have been reported a menstrual and postmenstrual lymphoid and plasma cell infiltration of the mantle tissue (Ernst 33) and hyperemia with secretion in the ducts during menstruation.

On account of these conflicting views, it became necessary to study independently a new series of breast sections in relation to the menstrual cycle. Accordingly 41 cases have been collected in which grossly normal tissue was removed from the breast at the time of the excision of a breast tumor The position in the cycle was determined from the history of the first day of the previous menstruation and in most cases of the succeeding period as well. The material is concededly inferior to certain previous studies in that the tissue was taken in the neighborhood of a definite disease process, from variable parts of the breast and was stained only by a routine hematoxylin-eosin method. It affords at least a basis for an intelligent evaluation of the existing mass of contradictory data.

In order to determine if possible the histological basis of abnormal premenstrual breast changes, the cases have been divided into those with and those without premenstrual pain or swelling For each case a tabulation was made of the average number of acini per lobule, the number of lobules per low power field, the presence of intracellular or extracellular secretion the definition of the lobule the character of the intralobular connective tissue and the degree of lymphoid infiltration. The material used is shown in Table I.

The chief feature of this series was the immediately evident variability of the lobular development in different breasts irrespective of the time of the cycle This is in direct accord with Dieckmann who recognized a

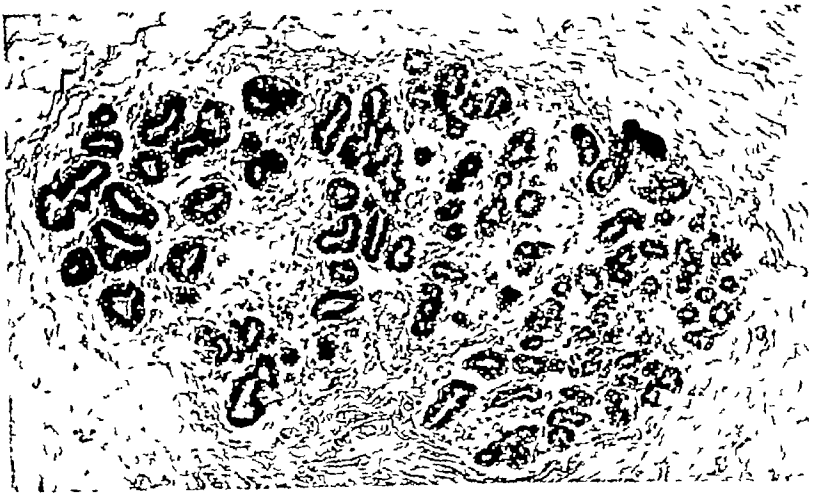

Fig 1 D5966 Well developed lobule with periacinar "edema" 3 days before the menstrual period Patient 40 years old, with 3 children, menstruating every 28 days for 5 days with slight 3 day premenstrual breast pain

mature and an immature type of lobule somewhat dependent on the patient's age This variability makes difficult attempts to prove the occurrence of premenstrual proliferation of the ducts by comparing single sections from different individuals, but makes it readily possible to arrange sections to illustrate any special morphological process that one may expect to find Taking Figures 1 and 2, one has the evidence to demonstrate the Rosenburg theory, but the reverse can be as readily shown, using Figures 3 and 4

A Epithelial changes The total disappearance of acini claimed by Rosenburg to take place in the interval must be a rare occurrence for in only 2 of the cases of the present series were acini largely absent Furthermore the average number of acini per lobule as determined by actual count of the cross sections of the acini of numerous gland fields did not show any consistent differences in women operated upon at different times in the cycle In particular it was interesting to note the persistence of acini and well developed lobules in the prolonged intermenstruum of women with cycles of 6 or 7 weeks (Fig 5), in the early menopause (Fig 6) and even several months after large doses of high voltage X-ray had been given to the ovaries (Fig 7) Finally in 1 case sections obtained by deliberate biopsy from identical parts of the two breasts on the fourteenth day of the cycle and again on the day of onset of menstruation showed

TABLE I —DISTRIBUTION AND SOURCE OF NORMAL BREAST SECTIONS

		Menstruation	Interval	Premenstruation
Cases without pain	Fibro-adenoma	2	5	2
	Chronic mastitis	1	4	0
	Carcinoma	3	0	1
Cases with pain	Fibro-adenoma	4	1	3
	Chronic mastitis	3	8	0
	Carcinoma	0	0	2
Total		13	18	10

Fig 2 E3640 Fibrosis of the lobule and apparent shrinkage of the acini on the fourteenth day of the cycle Patient 20 years old single, menstruating every 28 days for 5 days without premenstrual breast symptoms

Fig 3 D580 Slight acinar development and an differentiated intralobular connective tissue 3 days before menstruation Patient 3 years old, single menstruating every 28 days for 4 days without premenstrual breast symptoms

no definite differences in the degree of acinar development (Figs. 13 and 14)

Cyclical intracellular changes in the epithelium are probable for near the time of menstruation the individual cell outlines may be more distinct and the acini often appear larger and somewhat dilated whereas in the intermenstruum they are usually collapsed and inconspicuous. There is, however little mitosis to prove the actual formation of new epithelium nor when menstruation is over is there any massive desquamation of epithelial cells into the ducts. The degree and regularity of an epithelial cycle of proliferation and regression in the breast appears, therefore to have been exaggerated and its very existence to require better proof than has yet been submitted

B Connective tissue changes The premenstrual changes in the intralobular connective tissue received general confirmation in this series. Sections taken shortly before menstruation usually showed the connective tissue of delicate texture with its fibers widely separated giving the lobule a sharp outline against the dense general supporting tissue of the breast (Fig 1) In the intermenstruum the mantle tissue was coarse and dense and the outline of the lobule relatively indistinct (Fig 2) Nevertheless exceptions occurred both in the form of persistent lobular definition in the interval and nearly complete absence of connective tissue differentiation

Fig 4 F6700 Persistence of lobules with numerous acini on the thirteenth day of the cycle Patient 25 years old, married without pregnancies, menstruating every 28 days for 5 day with premenstrual tenderness and swelling of the breasts.

Fig 5 D2933 Persistence of acini in the interval of a prolonged cycle, 8 days after the previous menstruation and 35 days before the succeeding period Patient years old, married, thout pregnancies, menstruating every 5 to 8 weeks for 7 days without breast symptoms

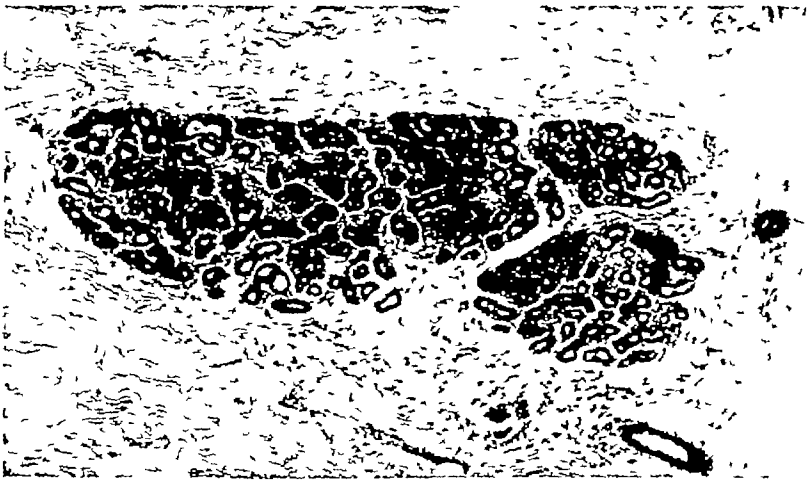

Fig 6 D3714 Persistence of acini in the early menopause, 6 months after the last menstrual period Patient age 47 married, childless, operated upon for localized chronic mastitis

shortly before menstruation The presence or absence of a round cell infiltration was in this series chiefly dependent upon the disease process for which the operation was undertaken

HISTOLOGICAL BASIS OF THE PAINFUL BREAST

Depending on the clinical appearance of the painful breast many of the older writers assumed that the changes had a vascular basis and were the result of venous congestion With the advent of belief in a premenstrual proliferation, the pain has been ascribed to an epithelial increase in the breast Rosenburg wrote "The sprouting by the rapidity of the growth causes the clinically noted tenseness in the breasts" Cheatle and Cutler, with the assumption that the painful breast is based on the pathological process which they term mazoplasia, ascribe the pain to a distention of the ducts with desquamated epithelial cells

Pain may occur in breasts which are essentially normal to palpation although in the more severe cases the breast is diffusely nodular In certain cases, furthermore, the pain may be localized in a single nodule This offers three types the histology of which must be considered

A The painful breast normal to clinical examination The breasts of a considerable

Fig 7 C4402 Definite lobules with persistence of acini 15 months after hysterectomy and 12 months after a castration dose of X-ray to the retained ovary The patient, a single woman of 43, with pain, nodules and enlargement following operation for myoma uteri.

Fig 8. E5901 "Edema" of lobule in a case of painful breast 2 days after the onset of menstruation Patient 36 years old, with a history of five miscarriages, menstruating every 1 days for 4 days with 7 days of premenstrual breast pain and heaviness

Fig 9 E5502 Normal breast tissue with premenstrual lobular edema, excised as a circumscribed lump 4 days before a menstrual period The patient an unmarried woman of 27 menstruating every 26 days for 6 days with an 8 day premenstrual and menstrual painful swelling of the breasts

percentage of all women are before the menstrual periods slightly swollen slightly sensitive with possibly a little evidence of hyperemia in the form of darkening of the areola and dilatation of the superficial veins.

For the study of this condition we have had to accept tissue removed at the time of an operation for fibro-adenoma from breasts grossly normal except for the circumscribed tumor and have for comparison 9 specimens from women without any premenstrual breast symptoms and 10 with premenstrual pain swelling or both The cases with symptoms showed a slightly more developed lobule as indicated by a count of the acini and in some cases a very pronounced "edema" of the mantle tissue (Fig 8)

This material, admittedly too small for final conclusions suggests that the common premenstrual breast symptoms occur in women with breasts at least fairly well developed who react somewhat more than the average to stimuli producing vascular dilatation and probably fluid changes in the interstitial tissue of the lobules

B The painful breast with diffuse areas of induration The patient who usually applies for treatment for the painful breast exhibits either a diffuse nodularity or particularly a nodularity of the upper outer quadrant This differs from a true tumor for its margins cannot be felt with the breast pressed flat against the chest but when the breast is raised and examined between the fingers a roughly circumscribed area often involving the whole upper outer quadrant can be readily outlined The nodularity is more marked before the menstrual periods and may be almost undetectible in the interval. The patient complains of pain beginning from a few days to 2 weeks before the menstrual period and often extending to the axilla, shoulder arm and over the lateral thoracic wall

Pathological sections of such tissue reveal a somewhat varied morphology so that one may conclude that many abnormal processes in the breast give pain under the influence of the hyperemia of the premenstrual phase. It is barely possible however that the different morphological appearances represent successive stages or local variations of a single basic process.

In one group of cases the histology shows little to distinguish the section from the normal Here one must conclude that the palpable abnormality represents a localized hypertrophy of all the tissues of the breast maintaining their normal relationships to each other or else that a vascular change such as a general slight edema has brought into sharp relief one part of the breast (Fig 9) A pathological report of chronic mastitis in such tissue is usually made on the basis of the clinical diagnosis.

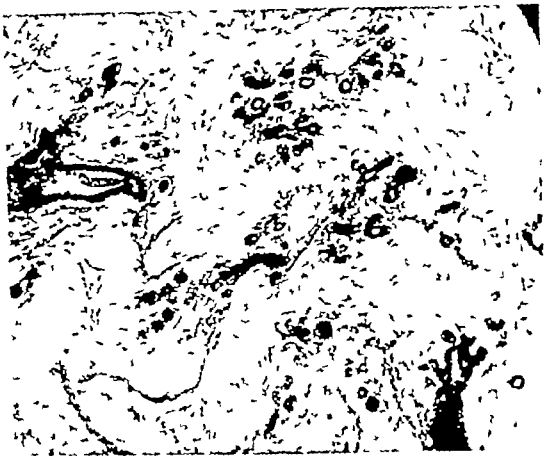

Fig 10 D3841 Fibrosis and distortion of lobule, twelfth day of cycle Patient age 45, married with 2 children menstruating every 28 days for 4 days, with premenstrual breast pain

In a second group of cases, there is a striking increase in the density of the connective tissue This may be apparent even in the gross in the texture of the breast tissue which is white, glistening, and fibrous with a disappearance of most of the adipose tissue between the lobules Under the microscope there is often a distortion of the normally well circumscribed lobules due to a fibrosis of the mantle tissue either by its local transformation or by an ingrowth of the coarse supporting tissue of the breast (Fig 10) In this group, there is little evidence of epithelial proliferation, and in many cases there may be an actual diminution in the size of the lobules and the number of acini

In a less frequent form there are signs of proliferation of the acini, so that the lobules are found close together, often coalescing, and the acini spread diffusely through the supporting tissue of the breast (Fig 11) Not infrequently this and the preceding type are combined and there is evidence of both glandular and connective tissue growth Finally the tissue removed from certain cases with pain may exceptionally exhibit the miscellaneous structures found in the more fully developed cases of Schimmelbusch disease such as cysts, adenomas of the sweat gland type, intraductal papillomas, and extensive round cell infiltration

Fig 11 E3928 Loss of lobular arrangement with diffusion of acini, fifth postmenstrual day Patient a woman of 38, married with 6 children, menstruating every 28 days for 2 days with premenstrual swelling of the breasts

C The histology of the circumscribed painful nodule The premenstrual breast pain may be localized in certain sharply circumscribed areas of the breast and over a period of months a lump may regularly appear during the week before menstruation and to a large extent disappear thereafter Such "disappearing lumps" may be found histologically to differ little from the normal breast tissue (Fig 9), or they may show an increase in connective or epithelial elements with a loss of the lobular outline On the other hand, typical fibroadenomas may also undergo the same premenstrual enlargement and increase of tenderness

HISTOLOGY OF THE HYPERTROPHIED BREAST

The hypertrophies of this series were for the most part minor degrees of permanent increase in size reported by the patient herself and not reaching obviously abnormal proportions Frequently the enlargement was

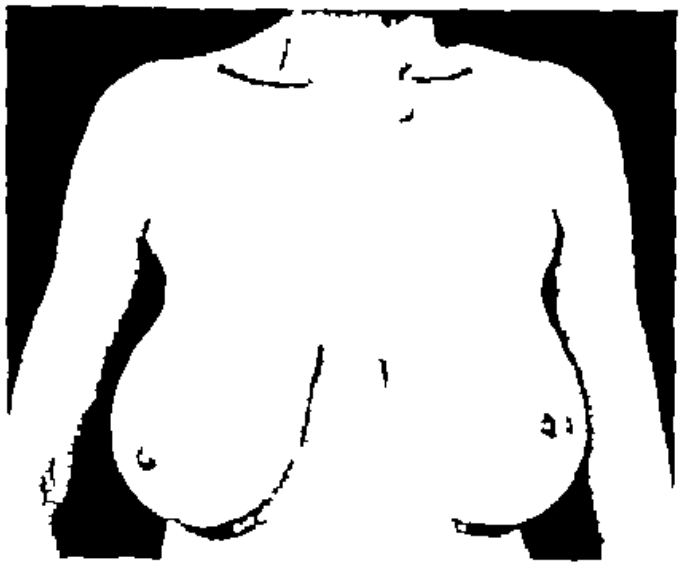

Fig 12 Premenstrual hemorrhages in the skin of the breast in a case of painful hypertrophy 3 days before menstruation. Patient divorced woman of 25 with a history of one miscarriage, menstruating every 5 to 6 weeks, for 3 to 5 days with scant flow, with severe dysmenorrhea and pronounced breast pain and swelling

unilateral and usually more marked in the outer quadrants sometimes giving the breast a distorted shape with the nipple displaced *toward the midline. Palpation showed as a*

Fig 13 (×10) Fibrosis and absence of epithelial hyperplasia in painful hypertrophy of the breast, section on the fourteenth day of cycle Patient the same as in Figure 2

rule distinct nodularity or circumscribed areas of induration in the tails. Pain and tenderness were always present sometimes so severe as to require sedatives to permit sleep

Premenstrual increase in the size and weight of the breasts again suggested congestion and hyperemia. The importance of the vascular factor was, however brought out most strikingly by one case in which areas of minute hemorrhages appeared in the skin of the breasts before each menstrual period (Fig 12)

This type of hypertrophy appears therefore to be closely related to the painful nodular breast and is clinically quite different from the painless hypertrophies seen in children (Frank, Bettinger Pahl Fasold Siegmund Novak) in the presence of ovarian tumors

The histological characteristics of these painful hypertrophies could be studied in only a few cases. In certain examples at least there is a marked increase in fibrous tissue giving a dense glistening white appearance *to the gross specimen a fact noted also in a* case described by Leriche (71) Under the microscope there may be large areas of connective tissue nearly free of glands and the few lobules are small with the acini separated by coarse fibrous tissue (Figs. 13 14) Much less commonly signs of epithelial proliferation and cysts may be present. The general picture corresponds closely with the description given for the histology of the painful breast

Fig 14 (×34 08) Fibrosis and absence of epithelial hyperplasia in painful hypertrophy section 5 hours after the onset of menstruation Patient the same as in Figures 2 and 3

HISTOLOGICAL BASIS OF THE NON-PUERPERAL SECRETING BREAST

Clinically there are several types of breast from which secretion can be expressed but they apparently fall into two principle groups

1 *Non-puerperal lactation* In this type the breasts are soft, usually non-painful, but with hyperemic areolæ and erect nipples The secretion is usually thin and has the cloudy appearance of colostrum but in marked cases it spurts from the ducts in the form of white opaque droplets of true milk The secretion of this type is nearly always bilateral There is no indication for operation and, although a number of such cases have been observed clinically at the Memorial Hospital, no histological material has been obtained

2 *Type associated with disease of the ducts* In the second type the secretion is less in amount and of varied character It may be serous, watery, oily, purulent, or somewhat inspissated so that it can be squeezed from the breast in worm-like coils The patient usually complains of pain which is less severe and more continuous than in the typical painful nodular breast The consistence of the breast with secretion may be fairly soft, or diffusely nodular, sometimes with the dense outer quadrant induration of the simple painful breast Occasionally dilated ducts are palpable beneath and around the areola Regular cyclical variations in the amount of secretion were not noted in this series

On gross section of such breasts, the ducts are found dilated and oozing with secretion, usually of the thick, semi-solid type Histological examination shows the ducts widened to cystic proportions and filled with granular amorphous material The lining cells are usually flattened and overlie a zone of connective tissue infiltrated with lymphocytes (Fig 14) Increase and diffusion of the acini with frequent dilatation of the smaller ducts is common toward the periphery of the breasts Finally with secretion from the nipple one may encounter marked proliferative activity of the duct epithelium, occasionally filling the lumina with solid masses of cells or developing papillomata (Fig 15)

TERMINOLOGY

The name of "chronic mastitis" on account of its familiarity has been retained in this paper as a general designation for the diffuse breast diseases associated with pain or discharge The term is not a good one, but appears as useful as such recently proposed names as "mazoplasia" or "cyclomastop-

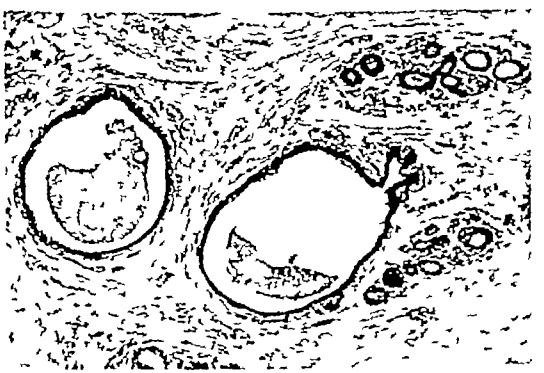

Fig 15 D5169 Dilatation of ducts with retained secretion in a case with secretion from the nipple, section on the twelfth day of the cycle Patient 39 years old, menstruating every 35 days for 4 days with premenstrual pain and swelling of the breasts

Fig 16 D2803 Polypoid adenomas of the sweat gland type from a case with a serous discharge from the left nipple. Patient a married woman of 24 with one child menstruating every 22 days for 6 days with severe cramps and intermittent pain and swelling of the breasts

athy The history of uterine nomenclature has shown a similar evolution from terms with suffixes indicating inflammation such as chronic endometritis" and adenomyositis, through the noncommittal metropathia, to the more anatomical terms, "hyperplasia and adenomyosis." A general word which accurately describes the basic changes in the common types of diffuse breast disease and which is in harmony with nomenclature used elsewhere in the reproductive tract is adenofibrosis. The term is similar to the word, "fibro-adenomatosis, adopted by Semb after his extensive histological studies

SUMMARY ON HISTOLOGICAL CONSIDERATIONS

The difference of opinion expressed by various observers and the easily found exceptions to the Rosenburg conception indicate that the cycle of a general premenstrual epithelial proliferation and postmenstrual regression has probably been exaggerated

A premenstrual hyperemia of the breast is however obvious from the gross changes in the size and the weight of the breast and the deepening of the color of the areola Microscopic evidence of this vascular change is found in the greater definition of the lobule and in the alteration of the character of the intralobular connective tissue.

The painful breast in its simplest form exhibits an increase in these premenstrual vascular changes. To refer the abnormal premenstrual swelling of the breast to excessive epithelial proliferation or the pain to the distention of the ducts with desquamated cells is contrary to many histological observations

The tissue in the milder forms of the painful breast may therefore appear almost normal under the microscope or may show excessive edema of the intralobular connective tissue In the cases with pain and marked nodularity there may be evidence also of irregular fibrous tissue and epithelial proliferation.

The histology of the painful hypertrophies of this series was in general similar to that of the painful nodular breast.

The histology of the breast with discharge from the nipple is variable and includes duct dilatation stasis, and catarrhal inflammation, frequently with secretion and hyperplasia of the epithelium and fibrosis and round cell infiltration of the connective tissue

NOTE —The second part of this study to be printed in the following issue of this journal will contain the results of a clinical and laboratory investigation of 161 women with these types of breast disease The data to be presented will include the record of menstrual types and anatomical conditions found in the pelvic organs, notes on the gross appearance of the ovaries and the histology of the endometrium in certain of these cases in which pelvic operations were performed and the result of biological tests for certain ovarian and pituitary hormones in the blood and urine of further group of patients

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THE INFLUENCE OF PEPSIN AND HYDROCHLORIC ACID ON THE HEALING OF GASTRIC DEFECTS

Artificial Gastric Ulcer

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PREVIOUS experimental attempts to prevent healing of the stomach after injury by the administration of hydrochloric acid have met with indifferent success The literature on this subject was recently reviewed in our publication on the relationship of the subcutaneous injection of histamine to the healing of mucosal defects (4) To our knowledge, however, the effect of the administration of pepsin has not been studied In these experiments, therefore, we have administered excessive amounts of pepsin and hydrochloric acid to animals with mucosal defects in the stomach and have observed the rate and character of healing The results will be compared with the healing of similar defects in a group of animals receiving equal amounts of hydrochloric acid without pepsin and with controls receiving neither acid nor pepsin

METHOD

Adult cats were used, ranging in weight from 2 8 to 4 5 kilograms Under ether anesthesia and through a gastrostomy wound a 1 square centimeter defect was cut in the mucosa of the posterior wall of the antrum, 1 to 3 centimeters from the pylorus, and the underlying muscle was scarified Beginning on the day after operation 1 to 3 doses of hydrochloric acid and pepsin, or of hydrochloric acid alone, were administered daily by stomach tube The doses given, 65 to 75 cubic centimeters, were put in the stomach at hourly intervals for it had been determined that this amount would remain in there for about 60 minutes Thus the maximum exposure of the defect to the administered acid or acid plus pepsin was attained The animals were allowed to eat a mixed laboratory diet The food was removed early enough before the solutions were given to allow the stomach to empty and returned to the cage after sufficient time had elapsed for them to leave the stomach With this scheme of feeding, food did not interfere with the action of the pepsin or of the acid When the cats were killed at the various intervals, their stomachs were distended with formalin and studied grossly and microscopically for disturbances of healing

The concentration of hydrochloric acid given to the majority of the cats ranged between hydrogen-ion concentration 1 0 and 1 4 This range of acidity is about equivalent to that for the gastric secretion obtained from the cat by stomach tube after histamine stimulation Chart I represents the average secretion in four cats resulting from the injection of two milligrams of histamine per kilogram The hydrogen-ion concentrations of these secretions determined colorimetrically varied between 1 0 and 2 0 Concentrations of acid above and below this range were also given to a few animals In the absence of data on the physiological variations in pepsin content of the gastric secretion of the cat, a wide range of

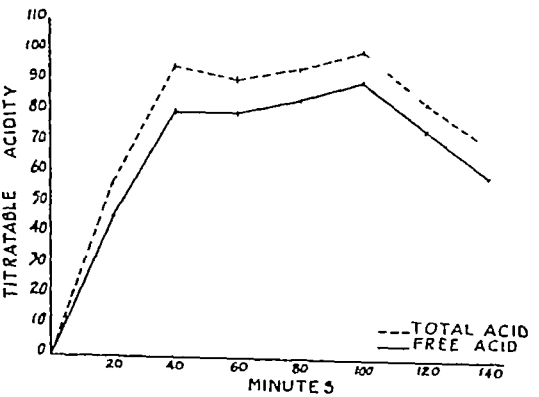

Chart 1 Average acidity of gastric secretion in four cats after 2 milligrams of histamine per kilogram Average individual volume of secretion was 60 cubic centimeters Hydrogen ion concentration varied from 1 0 to 1 6 Interrupted line, total acid, straight line, free acid

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TABLE I—HEALING OF PREPYLORIC DEFECTS WITH ACID ALONE

Cat No	Acid pH	Amount c.cm	Estimated minimal length of time in stomach per day (hours)	Days	Number of experiment after hr	pH of unsuspected juice	Results
		65 b.d.		7	Not done		Normal healing
	[illegible]	65 b.d.		7	Not done		Normal healing
3		65 b.d.		7	Not done		Normal healing
	[illegible]	65 b.d.		7	[illegible]		Normal healing
5		65 b.d.		7	6, returned	[illegible]	Moderate surface exudate
6		75 b.d.		13	7 returned	[illegible]	Healed
7		75 b.d.		7	1, returned		Normal healing
8		75 t.i.d.	3	14	Not done		Healed
9		75 t.i.d.	3	7	Not done		Normal healing
		75 t.i.d.	3	10	Not done		Normal healing
	9	75 b.d.	36	13	hr 36 hrs.	[illegible]	Open lesion—Healing delayed
	9	75 b.d.	48	3	36 hrs	[illegible]	Open lesion—Healing delayed
13	9	75 b.d.	36	14	hr 36 hrs.	Free acid present [illegible]	Open lesion—Healing delayed

concentrations varying between 0 05 to 2 per cent of pepsin 1 10,000 (Armour's) was used

RESULTS

The healing of mucosal defects in the stomach of the cats receiving neither acid nor pepsin was as follows At 1 week, epithelization had begun and at 2 weeks the lesion was completely closed. Because of the difficulty however of destroying the same amount of tissue at each operation, 5 more defects were cut deeper in order to evaluate the effect of a greater destruction of tissue on the healing process. These lesions were likewise studied after 1 week of healing and although some still had a small amount of surface exudate present, in most instances epithelium was beginning to form and the fibrous tissue had already regenerated (Fig 1) In comparing the lesions exposed to acid and pepsin therefore interference with healing was not considered noteworthy unless the surface exudate was more marked than in these controls. With this precaution misinterpretation caused by inevitable variations in the size of the original defect was avoided.

THE EFFECT OF HYDROCHLORIC ACID ALONE ON THE HEALING OF THE DEFECT

Either two or three times per day 13 animals received between 65 and 75 cubic centimeters of hydrochloric acid per dose. The details of the amounts given and the hydrogen-ion concentrations are shown in Table I These cats ate well, and their weights were maintained Seven of these receiving acids with hydrogen-ion concentrations varying from 1 1 to 2 were killed after 1 week. The lesions in their stomachs had undergone less contraction than had controls, and although histologically there was a small amount of surface exudate still present, yet only in one animal (No. 5) was the delay of healing more marked than had occurred in the controls (Figs. 2 and 3) Three other animals receiving acid alone of hydrogen ion concentration 1 1 to 1.2 were killed after longer periods of time on the thirteenth and fourteenth days of healing At 10 days epithelization was progressing normally and at 13 and 14 days the defects were covered with regenerated epithelium. On the other hand, all the lesions in 3 animals receiving acid of a hydrogen ion concentration of 0 9 killed after 13 or 14 days of healing showed a frank delay of the process Grossly these lesions were open to about half the original size and indurated but microscopically healing although retarded was definitely taking place.

To summarize then the administration of hydrochloric acid of hydrogen ion concentration 1 1 or greater had little or no effect upon the healing of the mucosal defect whereas

TABLE II—ACID PLUS PEPSIN

Cat No	Conc of pepsin (%)	pH	Amount (c.cm)	Average exposure per day	Days	Number of aspirations after 1 hr	pH of reaspirated juice	Results
14	0 05	1 2	65 b d.	2 hrs.	7	3, no return		Slight surface exudate
15	0 1	1.4	50 b d	2 hrs	7	Not done		No surface exudate
16	0 1	1.4	50 b d	2 hrs	7	Not done		Slight surface exudate
17	0 1	1.4	70 b d	2 hrs	7	Not done		No surface exudate
18	0 1	1.4	75 b d	2 hrs	7	Not done		Slight exudate
19	0 2	1 2	65 b d	2 hrs	7	2, return		Slight exudate
0	0 2	1 2	65 b d	2 hrs	7	7, return	1 4 1 6 2 2, 1.4	Moderate exudate
21	0 4	1 2	65 b d	2 hrs.	7	Not done		Moderate exudate
2	0 4	1 2	75 b d	2 hrs.	7	Not done		Moderate exudate
23	0 4	1 1	75 t.i d	3 hrs	7	3, return		Perforation
24	0 4	1 2	75 t.i d	3 hrs	7	Not done		Extensive surface exudate
25	0 4	1 1	75 t.i d.	3 hrs	9	2, return		Moderate exudate
6	0 4	1 1	75 t.i d.	3 hrs	10	5 return		Perforation
27	0 4	1 1	75 t i d	3 hrs	10	Not done		Marked surface exudate
28	0 3	1 2	75 t.i d	3 hrs.	13	Not done		Very little healing
29	0 4	1.4	75 b d	2 hrs	13	5, return	1.4, 1 6 1 6 1 7, 1.4	Almost covered with epithelium
30	0 4	1 2	75 t i.d	3 hrs.	13	Not done		Almost covered with epithelium
31	1	1 1	65 t i d	3 hrs.	13	1, return		Almost covered with epithelium
32	0 2	1 1	65 t i d	3 hrs.	14	3 return	1.4	Covered with epithelium
33	0 4	1 2	75 t.i d	3 hrs	14	1 return		Almost covered with epithelium
34	0 2	1 0	75 t.i d	3 hrs	14	7, return	1 6 1 6 1 2 1 8 1 5, 1.4	Almost covered with epithelium
35	0 4	2 0	65 b d	1 hrs	7	Not done		Slight surface exudate
36	0 1	2 8	65 b d	1 hr	7	Not done		No surface exudate
37	0 4	0 9	75 b d		14	1¾ hrs 1½ hrs	Free acid present Free acid present	No surface exudate
38	0 4	0 9	75 b d		14			Open lesions
39	0 4	0 9	75 b d		14	1½ hrs. 1¾ hrs	94–106 m eq 94–114 m eq	Open lesions Open lesions

acid of a hydrogen-ion concentration 0 9 did delay healing

THE EFFECT OF PEPSIN AND HYDROCHLORIC ACID ON THE HEALING OF THE DEFECT

Twenty-six animals received artificial gastric juice containing hydrochloric acid and commercial pepsin (1 10,000 Armour) (Table II) The doses given varied between 50 and 75 cubic centimeters, and the pepsin content ranged between 0 05 and 1 0 per cent The hydrogen-ion concentration of the mixtures extended from 0 9 to 2 8 Two or three doses were administered daily The animals which received two doses daily ate fairly well and remained in good condition while those receiving three doses occasionally vomited and had a coincidental loss of appetite and weight Twelve of these cats were killed after 1 week of healing, and four of the defects showed considerable interference with healing, i e, slough in the floor of the defect grossly and microscopically an abundant polymorphonuclear exudate on the surface and absence of growth of epithelium at the edges (Figs 4 and 5) One animal died of a perforated ulcer on the seventh day (Fig 6) Five other lesions in this group likewise showed some surface exudate, but inasmuch as the amount did not exceed that seen in the controls, no significance was attached to it The lesions in the 2 remaining animals showed normal healing, but

TABLE III—CATS RECEIVING EPHEDRINE AND ARTIFICIAL GASTRIC JUICE

Cat No.	Gastric juice	Amount of ephedrine per kilogram	Calculated loss of peptic activity per day	Recuperations several hours after ingestion	Days	Results
40	Pepsin [illegible]% pH [illegible] 75 cm [illegible]	3 mgm	[illegible]	3 hrs.—free acid 3 hrs.—none	7	Marked surface [illegible]
41	Pepsin [illegible] pH [illegible] 75 cm [illegible]	3 mgm.—7 days none 7–14 days	[illegible]	3 hrs.—pH 3 3 hrs.—none	9	Healed
42	Pepsin [illegible]% pH [illegible] 75 cm [illegible]	3 mgm.	4	hrs.—pH 3	14	Healed
43	Histamine subcutaneously [illegible] mg/kg	3 mgm		3 hrs.—free acid 3 hrs.—none 3 hrs.—free acid	14	Open healing
44	Pepsin [illegible]% pH [illegible] 75 cm [illegible]	mgm	4+	3½ hrs.—free acid 4 hrs.—none 3½ hrs.—free acid	3	Open healing
45	Pepsin [illegible]% pH [illegible] 75 cm [illegible]	3 mgm	3+	3½ hrs.—pH [illegible] 3½ hrs.—pH [illegible] 4½ hrs.—free acid 3½ hrs.—free acid	3	Open healing

these cats received in one instance a weak concentration of pepsin and in the other the acidity was weak (No. 36)

Healing was allowed to continue for a longer period of time in the 13 other animals. One was killed on the ninth and another on the tenth day and each showed marked interference with healing. A third animal died of a perforated lesion on the tenth day The 10 other animals were killed on the thirteenth or fourteenth days and the defects in their stomachs had started to heal. Histologically there was a thin single layer of regenerating epithelial cells growing in from the margins and it was evident that the lesions would be completely covered in a few more days None had the marginal gastritis seen around the chronic gastric ulcer in the stomach of man.

In general then the defects in the animals receiving pepsin and acid showed greater delay of healing than did those in the animals receiving acid alone. The effect was most marked when the acidity approached tenth normal (pH 1.0) and with pepsin of 0.4 per cent. On the other hand the same concentration of hydrochloric acid alone had had little or no effect upon healing The presence of pepsin in sufficient concentration, therefore enhances the destructive action of gastric juice and causes a longer delay of healing.

DURATION OF EXPOSURE OF INJURED STOMACHS TO ACID PLUS PEPSIN

Numerous preliminary observations were made on the rate of emptying and of neutralization of the various volumes and concentrations of acid introduced into the cat s stomach The findings confirmed in principle the reports of other observers (2) on the fate of acid after introduction into the stomach. In general the acidity was progressively reduced and the time when the fluid finally left the stomach depended on the hydrogen-ion concentration of the solution. Weaker concentrations of acid left the stomach more rapidly than those of greater acidity Thus with 75 cubic centimeters of hydrochloric acid of hydrogen-ion concentration of 1 2 a small amount could be recovered at the end of 1 hour and the acidity had decreased to a hydrogen-ion concentration between 1.4 and 2.0 while with the same volume of acid of hydrogen ion concentration 2.0 introduced none could be recovered at the end of one-half hour The addition of pepsin to the acid did not alter these changes.

In order to determine the change in peptic activity of the pepsin hydrochloric acid mixture after being in the stomach for a period of time two cats were lightly anesthetized with nembutal and given 75 cubic centimeters of a 0.1 per cent solution of pepsin at a hydrogen-ion concentration of 1 1 The stomach content was then aspirated after 1 hour and the digestive activity determined by the method of Anson and Mirsky This test demonstrated that very little change in peptic activity had occurred. Moreover by aspirating the stomach of the animals with defects, we were able to show that injury had no effect on the length of time which the various solutions remained

Fig 1 Character of healing of prepyloric defect after 1 week in stomach of a control cat. The muscularis has been deeply scarified There is a small amount of surface exudate

in it or that the changes which occurred in the acidity differed in any way The details of these findings are recorded in Tables I and II In the series which received acid alone, it will be noted that the exposure of the defect to acid ranging between hydrogen-ion concentration 1 1 and 2 0 was over 3 hours per day (animals No 8, 9, and 10) A similar period of exposure was also attained in those animals which received pepsin hydrochloric acid of the same acidity (Animals Nos 23, 24, etc)

THE EFFECTS OF LONGER EXPOSURE OF GASTRIC JUICE ON THE HEALING OF THE MUCOSAL DEFECTS

To retain the acid pepsin mixture in the stomach for longer periods of time, coincident injections of ephedrine sulphate were given This drug decreases peristalsis With 3 to 4 milligrams per kilogram administered subcutaneously, the solutions remained in the stomach two to four times longer than without it Five animals (Table III) received solutions of pepsin hydrochloric acid and also simultaneous injections of ephedrine sulphate The solutions given were of hydrogen-ion concentration 1 0 to 1 2 with pepsin of 0 4 to 2 0 per cent Two animals received one dose of the artificial gastric juice and ephedrine per day, and 3 received two doses of each The stomach of one of the former animals was examined at the end of 1 week, and the lesion showed marked interference with healing comparable to that seen with 3 hours' exposure to the acid and pepsin mixture obtained without ephedrine The 4 remaining animals were killed after 2 weeks, and 2 had open but healing defects while the others were already covered with epithelium Another animal included in this series received 2 milligrams of histamine—a dose which we have previously shown is effective in delaying healing—and 5 milligrams of ephedrine per kilogram for 2 weeks When the animal was killed, however, the lesion, although open, was likewise healing

Aspiration of the stomachs of these cats receiving ephedrine indicated that a single dose of acid and pepsin remained in the stomach for as long as 3½ to 4 hours and that the rate of change of hydrogen-ion concentration was also slower than in the cats not receiving ephedrine With 75 cubic centimeters of hydrogen-ion concentration 1 1 fluid could still be aspirated at 3½ hours, and it still had a hydrogen-ion concentration of 1 6 (No 45) (Table III) Thus with two doses of the artificial gastric juice and ephedrine, the lesion was in contact with the acid and pepsin for 6 to 8 hours, but in spite of the prolonged daily exposure, the healing of the mucosal defects showed no tendency to become chronic

Lastly, in order to eliminate the possibility that the gastric juice of the patients with chronic ulcer might contain some substance which affects the healing of mucosal defects in

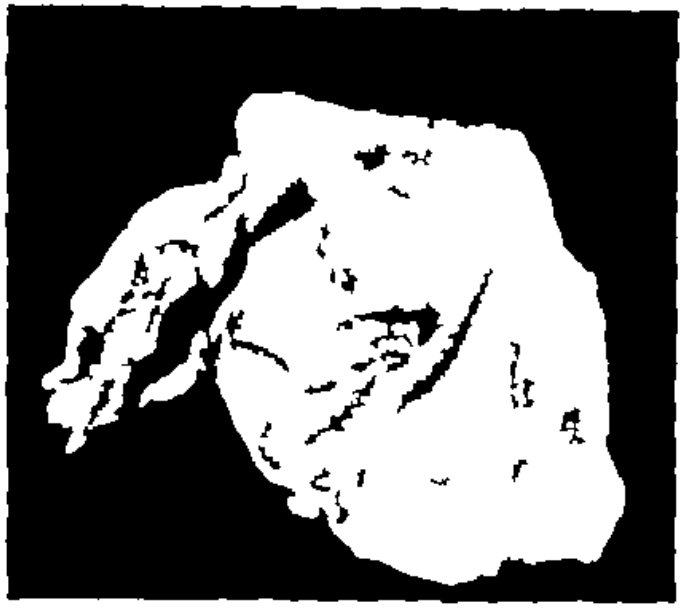

Fig. 2. Prepyloric defect in cat's stomach showing effect per day for 7 days of 75 cubic centimeters of hydrochloric acid of hydrogen ion concentration. The lesion is wider than in controls, but otherwise healing is normal.

such a way that chronicity results, two animals with prepyloric defects were given 75 cubic centimeters twice a day of gastric juice from patients with active peptic ulcer. The juice was taken during fasting and after histamine. *One of these animals killed after 7 days of* healing had a defect with a slight surface exudate and the other was epithelialized after 14 days.

EVALUATION OF STUDY

Hydrochloric acid alone in high concentration has a destructive action upon a denuded area of the stomach and delays healing. Under the conditions of our experiments acid of a hydrogen-ion concentration of 0.9 was required. Delay was not obtained with a hydrogen-ion concentration of 1 or greater. The addition of pepsin, however, to the hydrochloric acid of the weaker concentrations *was followed in some instances by* marked tissue destruction and delay of healing. It appears therefore, that gastric juice may have an injurious effect upon an open lesion of the stomach in two ways: by the direct corrosive action of the acid and by the digestive action of pepsin. The extent of the damage, of course, is dependent on the concentration of pepsin and acid in either case.

Anatomically the picture in both instances is one of tissue necrosis and acute inflammatory reaction. When the necrosis is maximal, moreover, perforation of the stomach may occur as it did in several animals in our series. This necrosis is the cause of the delay of healing, for fibroplasia and epithelial regeneration once started were not prevented by continued corrosive or digestive actions. Thus although the acid plus pepsin and acid alone were given everyday, the regeneration of epithelium and fibrous tissue took place unabated *from the seventh to the fourteenth day* of healing.

No evidence was obtained which would indicate that gastric juice could cause an acute lesion in the otherwise normal stomach to become a chronic ulcer. Increasing the concentration of pepsin many times or the length of daily exposure of the lesion to

Fig. 3. Character of healing with two doses daily for 7 days, of hydrochloric acid of hydrogen ion concentration. *Surface exudate is present but very* small in amount. Spread of epithelium more extensive.

strong digestive juice did not result in a corresponding increase in the time required for healing to take place It is possible, however, that ephedrine may have antagonized the effect of the gastric juice in some way The experiments with the transferred gastric juice from patients with chronic ulcers suggests also that there is no mysterious substance secreted into the stomach of the patient which causes chronicity

On the other hand, the failure of these experiments to produce chronic ulcers need not cast doubt upon the usual clinical concept of the causal relationship between gastric juice and the chronicity of ulcer It must be remembered that the stomach has many ways of defending itself against the digestive action of gastric juice and that some of these were in no way disturbed by our methods Thus, the length of time in which the juice remains in the stomach, its hydrogen-ion concentration and peptic activity are influenced by the intensity and frequency of the peristaltic waves, by the relaxation of the pyloric sphincter, and by the rate of neutralization by alkaline juices Mucous and some living principle of the cell generally termed "antipeptic" are likewise involved It is conceivable therefore, that further interference with these protective mechanisms in the patient's stomach might account for a greater susceptibility of the open lesion to the action of pepsin and hydrochloric acid and explain the chronicity of peptic ulcers That there is some relationship between the gastric juice and the chronic state of the peptic ulcer is suggested, of course, by the healing of some ulcers by therapeutic neutralization with alkalies taken by mouth and by the shortening of the emptying time of the stomach by surgical procedures Furthermore, the human stomach with chronic ulcer

Fig 4 Character of healing on the seventh day of a prepyloric defect in the stomach of a cat receiving 2 doses per day of artificial gastric juice of hydrogen-ion concentration, 1 2, pepsin, 4 per cent (1 10,000) Lesion was indurated The gross appearance of the surrounding stomach suggests gastritis but histologically it was not present.

Fig 5 Character of healing with 2 doses daily of artificial gastric juice for 7 days Note extensiveness of surface exudate although the muscularis is not as deeply scarified as in Figure 3 Epithelium is beginning to regenerate on the left

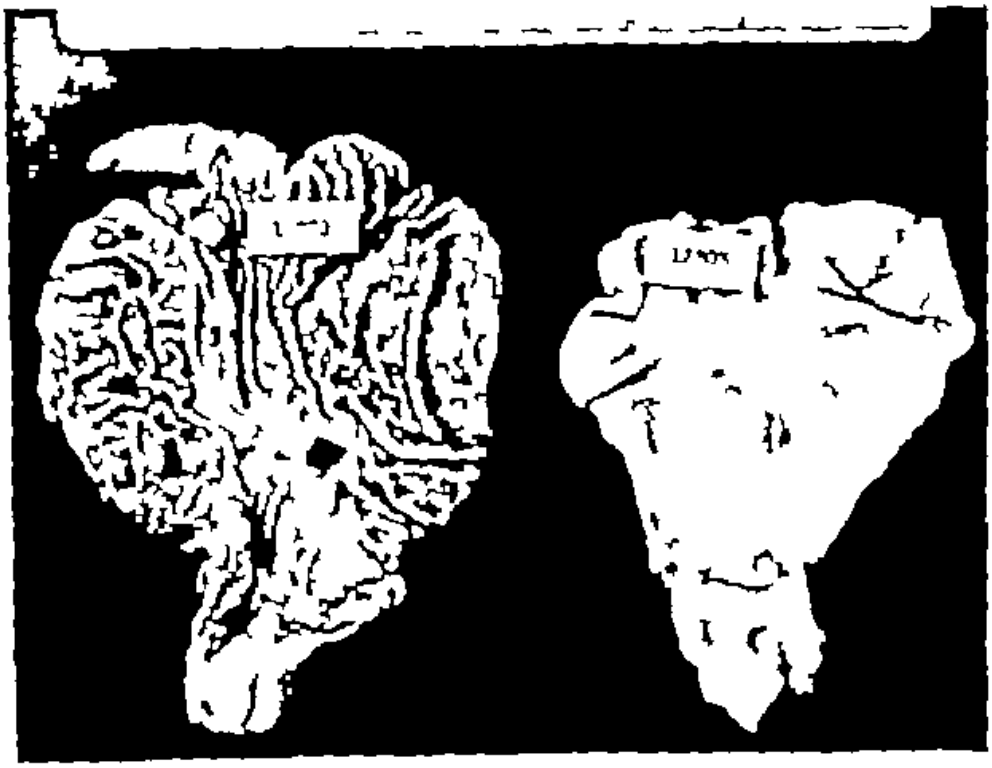

Fig 6 Left, perforated prepyloric defect on seventh day following administration of 75 cubic centimeters of artificial gastric juice of hydrogen ion concentration, 2, pepsin 4 per cent three times a day

Right, 75 cubic centimeters of hydrochloric acid of hydrogen ion concentration, 2, three times day for 7 days Healing is within normal limits

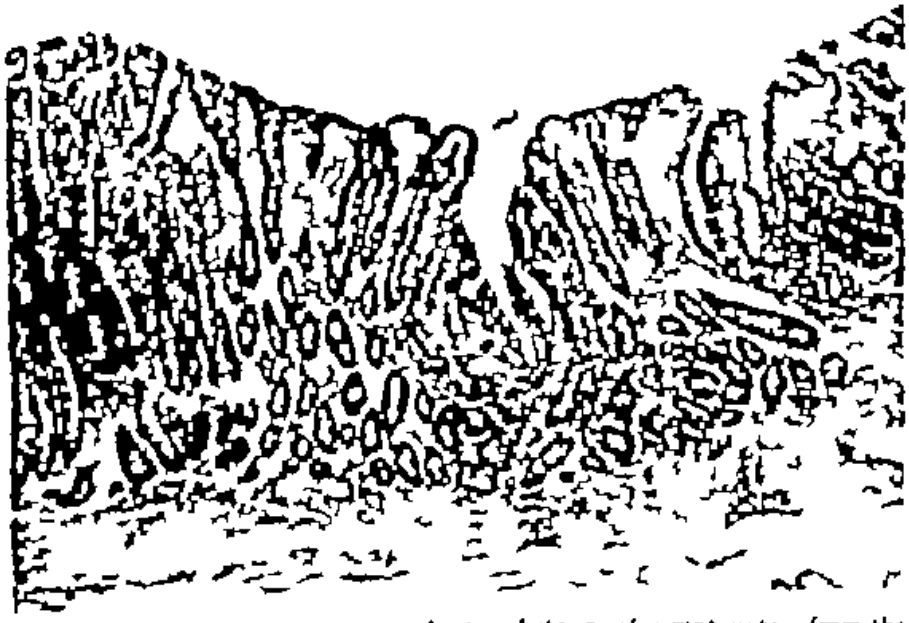

Fig 7 Gastritis in human stomach 1 a distance of 5 centimeters from the margin of the ulcer There are numerous goblet cells, the glands are arranged irregularly and there is cellular infiltration In spite of prolonged exposure to strong gastric juice changes of this character have not been produced in the stomach of the cat

shows general evidence of insult and there is no data to indicate that this gastritis is not caused by some disturbed relationship between the corrosive and digestive activity of the content on the one hand and the protective mechanisms on the other Konjetzny particu-

larly has demonstrated these inflammatory or degenerative changes at a distance from the site of the ulcer We have recently reviewed the specimens of 25 gastric resections done for gastric ulcer at this clinic and have likewise found microscopic evidence of gastritis at a distance from the ulcer in 80 per cent (Fig 7) There is also the possibility which must not be forgotten that this altered epithelium has less ability to regenerate in the presence of a potent digestive juice than has normal mucosa

From the clinical standpoint, the importance of an enhanced peptic activity of the gastric juice in patients with ulcer is illustrated by the experiments, and recently the findings of Vanzant and his collaborators have indicated that these individuals actually have a high pepsin content in their gastric juice However, these investigators found the increased amounts of pepsin in the patients with duodenal rather than gastric ulcers

In conclusion, on the basis of our experimental evidence, we feel justified in asserting that pepsin and hydrochloric acid causes the acute necrosis seen in the floor of the ulceration and that this necrosis may become sufficient at times to result in perforation On the other hand, with the methods used we were unable to obtain any evidence that gastric juice could cause an acute ulceration in an otherwise normal stomach to become a chronic ulcer

CONCLUSIONS

1 Instillation of hydrochloric acid of a hydrogen-ion concentration of 0 9 into the stomach of the cat delayed but did not prevent healing of a mucosal defect Acid of a hydrogen-ion concentration 1 or greater had little or no effect upon healing

2 Pepsin combined with the weaker concentrations of acid, however, caused marked necrosis of the floor of mucosal defect, and although healing was delayed, ultimately it was not prevented

3 The tendency toward chronicity in the healing of the defect was not increased either with longer exposure of the defect to pepsin-hydrochloric acid or by increasing the concentration of pepsin

4 The delay in healing of the defect with pepsin hydrochloric acid or with strong hydrochloric acid without pepsin was caused by the acute necrosis of the floor of the defect The regeneration of fibrous tissue or of epithelium once started was not prevented by repeated insults by these solutions

5 The failure of these experiments to produce chronic ulcers does not invalidate the clinical concept of the causal relationship between gastric juice and the chronicity of ulcer for the defense mechanisms against the action of potent gastric juice were relatively undisturbed in these investigations

6 The gastric juice of the patient with chronic peptic ulcer has no more capacity to cause an acute mucosal ulceration to become chronic than does artificial gastric juice

7 In general, the experiments indicated that the stomach, even when injured, has the ability to cope with destructive digestive juices remaining in the lumen for long periods of time provided the defense mechanisms are not too disturbed

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[illegible]

[illegible] may be [illegible] a healthy [illegible] tumors [illegible] [illegible] premonitory [illegible] may even [illegible] which throw a shadow [illegible] Fibroblastomas at the [illegible] as prone to invade the [illegible] hyperostosis as those [illegible] that they may do [illegible] are reported by Cushing and Eisenhardt [illegible] which tumor cells were found [illegible] the region of the tuberculum sellae [illegible] not common.

Unlike the [illegible] the blastomas are attached to the sella only at one or two points, usually the [illegible] sella and the sulcus chiasmatis. When these attachments [illegible] possible to remove these tumors if they [illegible] large dimensions. The [illegible] underlying the tumor is usually infiltrated with [illegible] tumor cells and unless removed [illegible] recurrences.

Because of the proximity to the optic nerves impairment of vision is almost invariably the

[illegible] symptom [illegible] the [illegible] impairment of vision [illegible] the [illegible] cases [illegible] symptoms [illegible] tumors [illegible] Case [illegible] reported.

Case [illegible] A woman [illegible] her [illegible] failing of [illegible] There [illegible] symptoms other than [illegible] of the [illegible] tumor [illegible] from the tuberculum sellae was [illegible] removed [illegible] discharge [illegible] in each eye.

Case [illegible] history. C [illegible] a female [illegible] was referred to the [illegible] service of the University Hospital [illegible] by Dr [illegible]. Five years before [illegible] the patient [illegible] attacks of vertigo [illegible]. There were [illegible] and in course of time [illegible] her [illegible] affected first in her right eye then in the left [illegible] the exception of some [illegible] in her [illegible] epoch [illegible] was the only [illegible] of the patient.

Examination. In every respect [illegible] her [illegible] apparatus the physical examination was [illegible]. In the roentgenograms the optic canals were [illegible]. There were no signs of pressure, no [illegible] of the clinoid processes. The sella turcica was [illegible] (Fig. 47) the basal [illegible] was [illegible]. The patient was a spare woman weight [illegible] pounds, with [illegible] hypophyseal stigmata. Vision, right eye [illegible] left eye 1/30. Fields—right [illegible] hemianopsia [illegible] discs yellow and pale. No papilledema. Presumptive diagnosis: suprasellar or sphenoidal [illegible] blastoma.

Operation. Transfrontal craniotomy [illegible] October 13, 1934. Through a coronal incision [illegible] exposed and removed a tumor which overlapped the anterior margin of the sella turcica and [illegible] optic nerves (Fig. 50).

Pathological diagnosis. Fibroblastoma.

Postoperative course. The patient made an uneventful convalescence and almost immediately after operation her temporal hemianopsia [illegible] apparent. Her vision on discharge was [illegible] eye as compared with 1/30 and 6/[illegible] on [illegible] (Figs. [illegible] and 5[illegible]).

[illegible]

Fig 48 A meningeal fibroblastoma from the suprasellar region showing the characteristic whorl arrangement Hematoxylin and eosin stain

Fig 49 Case 14 X ray of sella turcica in a case of suprasellar fibroblastoma Note sella not enlarged Measurements, anteroposterior, 11 millimeters, depth, 9 millimeters

CASE 15 A middle aged woman began to lose the sight of the right eye 6 years ago and in 4 years the vision in that eye was totally lost For 3 years the sight of the left eye had been failing Headaches are not a feature Intense drowsiness 2 years ago Left eye—temporal hemianopsia Both discs were waxy yellow A suprasellar fibroblastoma was found and removed

Clinical history E J B, aged 51 years (File No 8215), was admitted to the neurosurgical service of the University Hospital April 28, 1926 She was well apparently until 6 years ago when the vision of her right eye became blurred and in the course of the following 4 years vision in this eye was completely lost (Fig 53)

Three years ago a mist appeared before the left eye and now the patient can only distinguish large objects, as different pieces of furniture She has had occasional pain in the right frontal region, but no headaches except when tired During the past 2 weeks she had five attacks of nausea and vomiting

Her menstrual flow has become scanty, she has lost rather than gained weight and for some 2 years she has at times been extremely drowsy It was said that up to 2 years ago she had an excessive craving for meat

Examination The examination, with the exception of her visual defects and the appearance of the discs, was to all intents and purposes negative The metabolic rate was plus 6 There was but a slight atrophy of the posterior clinoid processes but the pituitary fossa was well within normal limits, 7 by 10 millimeters

Ocular findings Both discs showed a waxy yellow atrophy with well defined margins The right eye was blind The temporal field of the left eye was lost and on the nasal side she could distinguish only large objects

Operation May 10, 1926 Transfrontal craniotomy No increased intracranial pressure A hard, firm, encapsulated tumor the size of a plum was found directly over the sella (Fig 54), which proved on examination to be a fibroblastoma Subtotal removal Convalescence uneventful

Postoperative course The patient's convalescence was uneventful and when last heard from, September 11, 1930, she was in excellent health though she had almost lost the vision of the left eye

The suprasellar fibroblastoma takes its origin from the tuberculum sellæ and as it increases in size the tumor stretches and separates the optic nerves and displaces the chiasm

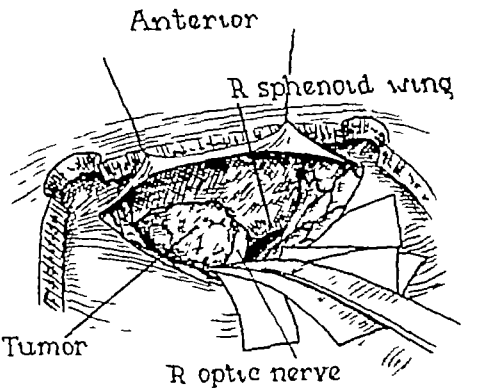

Fig 50 Case 14 Drawing of tumor as seen at operation, overlapping the anterior margin of the sella turcica

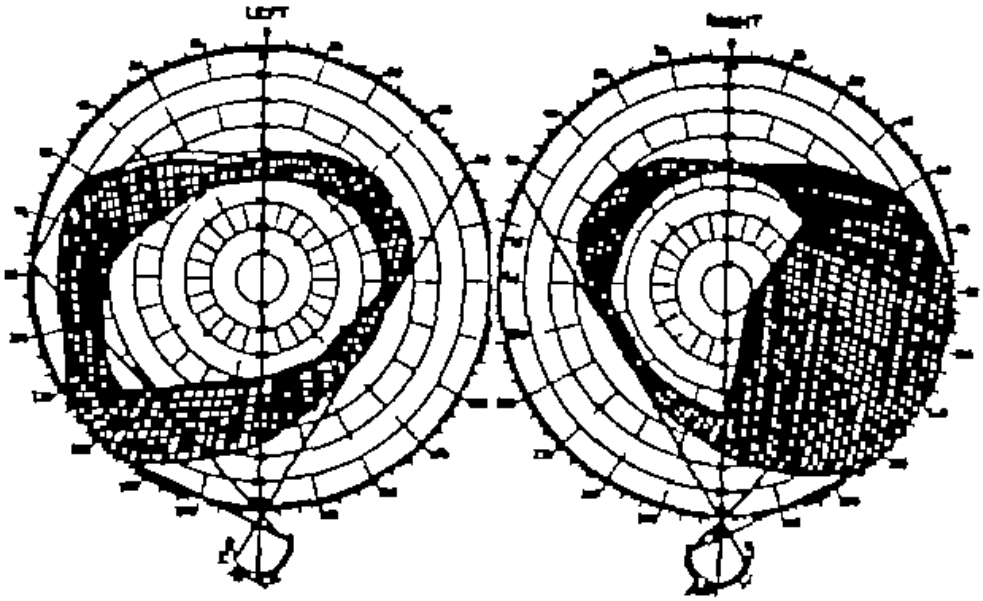

Fig 5 Case 14 Fields before operation Vision—left eye, /30 right eye, 6/30

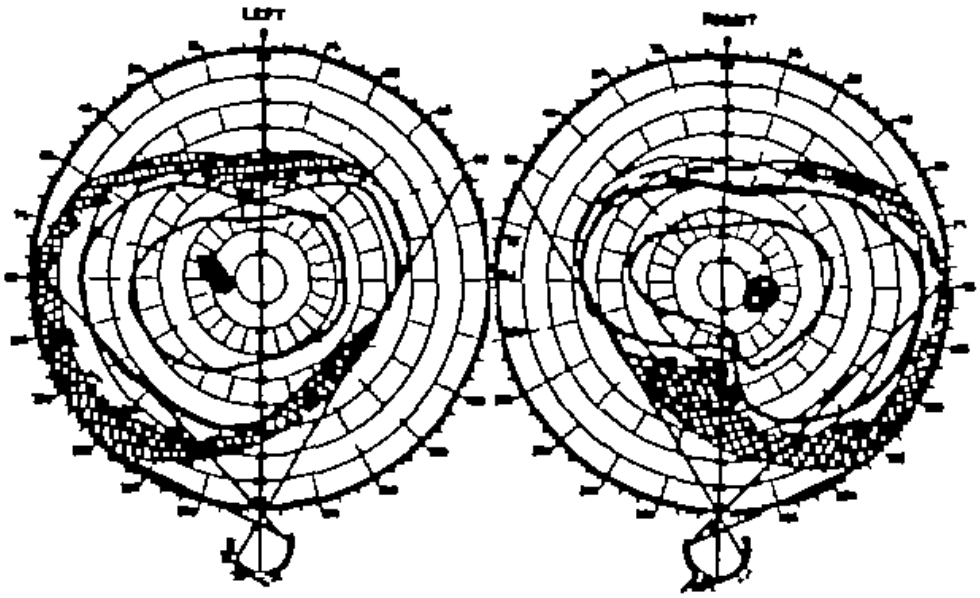

Fig 5a Case 14 Fields after operation. Vision—left eye, 6/9 right eye, 6/9

upward and backward. It is not associated as are other fibroblastomas with a hyperostosis nor will the roentgenogram reveal any enlargement of the sella turcica.

Obviously when the lesion is not promptly recognized—and years may elapse before the tumor is exposed at operation or discovered at autopsy—the tumor may be sufficiently large to cause neighborhood symptoms and changes in the sella turcica The latter may become eroded there may be uncinate attacks, convulsions, evidence of hypophyseal dysfunction and of hypothalamic damage. In a patient referred to by Holmes and Sargent, 11 years after beginning impairment of vision included in the picture were drowsiness, adiposity increased sugar tolerance headaches, dizziness and vomiting and the patient was completely blind One patient of our series (Case 15) had for 2 years complained of drowsiness so intense that it was difficult for her to keep awake In another (File No 11447) there was definite evidence of hypophyseal dysfunction In cases of more recent development (Case 14) there may be not the slightest evidence of an intracranial tumor

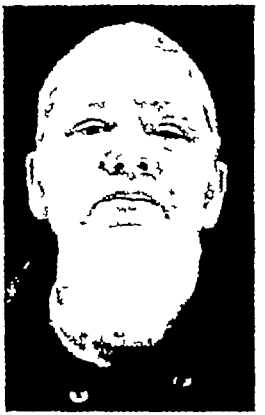

Fig 53 Case 15 Patient with suprasellar fibroblastoma The only symptom was blindness

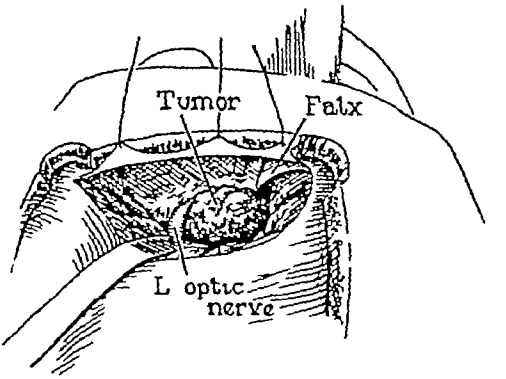

Fig 54 Case 15 Suprasellar fibroblastoma exposed at operation The left olfactory nerve has been divided

other than that attributable to pressure upon the optic nerves and chiasm This patient had no signs of hypophyseal dysfunction there were no signs of increased intracranial pressure, there were no neighborhood symptoms, and the roentgenogram was normal

How can these suprasellar fibroblastomas be differentiated from the other groups of parahypophyseal lesions? When it is a matter of differentiation from tumors of congenital origin, the stalk tumors the teratomas, the tumor of Rathke's cleft, there should be little confusion, especially if one remember that these tumors of congenital origin occur chiefly in children and adolescents, that the X-ray often reveals calcified shadows and some deformity of the sella. The primary intrasellar adenoma has earmarks so characteristic that a mistake in diagnosis would seem unpardonable On the other hand, the extrasellar or suprasellar adenoma may present a picture so like that of the suprasellar fibroblastoma that one may readily be mistaken for the other (see Case 16) Both occur in adults in both the sella is not enlarged, in both primary optic atrophy and temporal field encroachment are constant In neither may there be any evidence of hypophyseal dysfunction

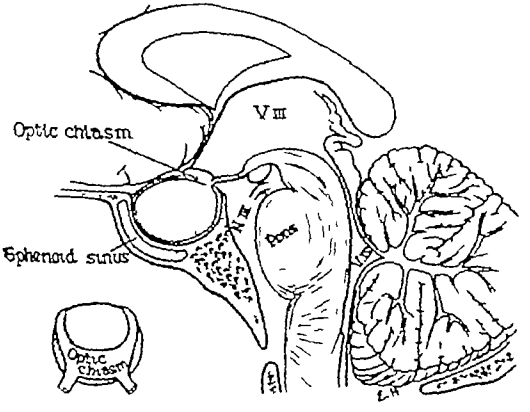

Fig 55 Large intrasellar adenoma with typical sellar deformity, a large ballooned out sella, with erosion of anterior clinoids, encroachment on sphenoid sinus and compression of optic nerves and chiasm.

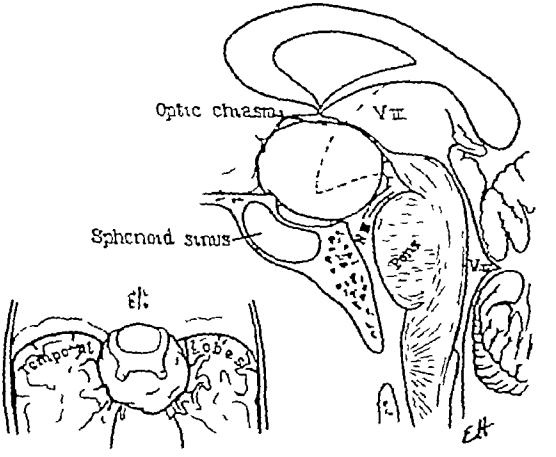

Fig 56 A suprasellar adenoma showing compression of the chiasm with the anteroposterior enlargement of the sella turcica but no encroachment on the sphenoid sinus The insert shows the tumor compressing the left oculomotor nerve and occupying the entire base of the brain between both temporal lobes

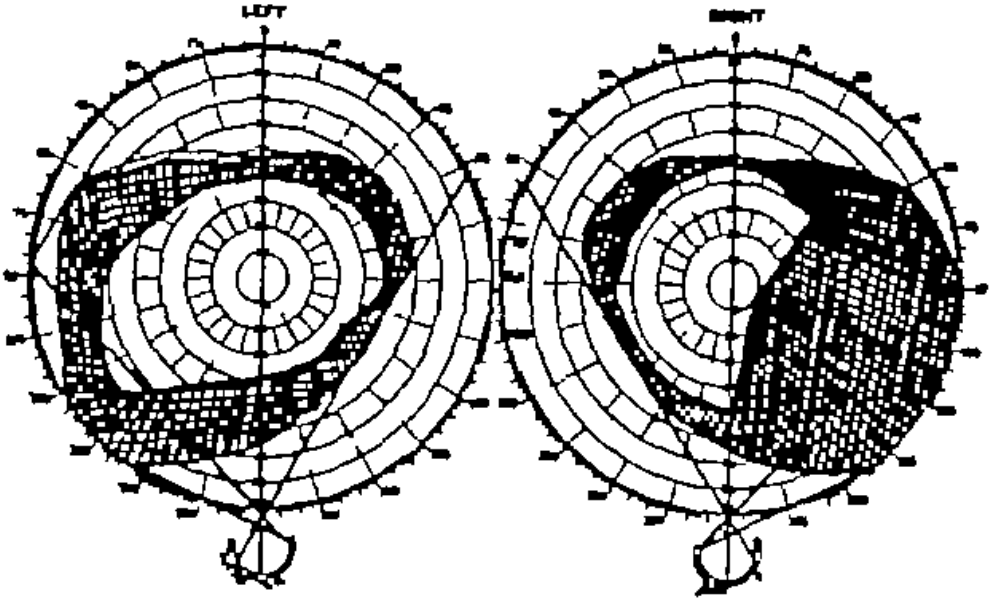

Fig 31 Case 14 Fields before operation Vision—left eye, /30 right eye 6/30

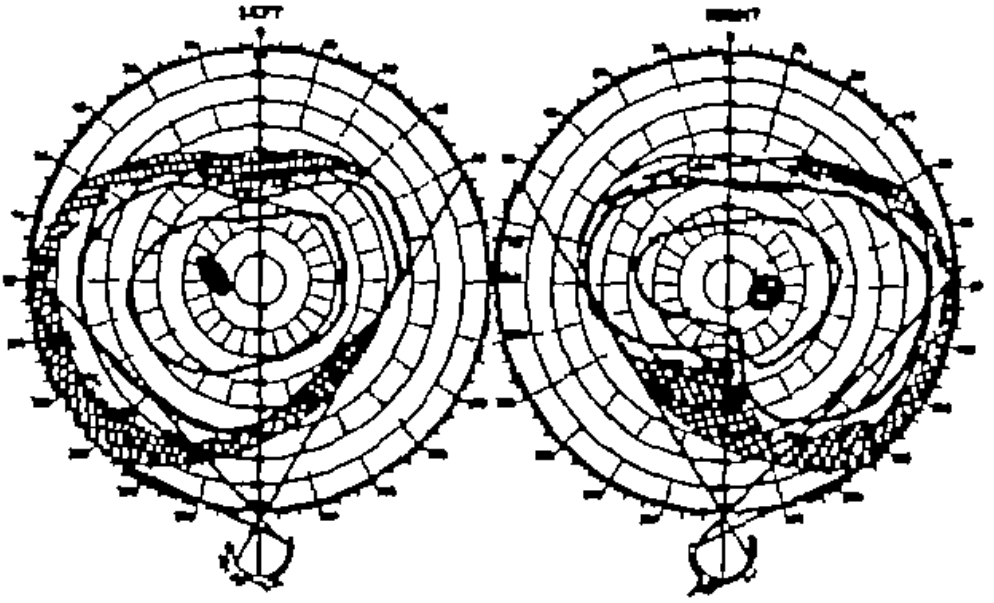

Fig 32. Case 14 Fields after operation Vision—left eye, 6/9, right eye, 6/9

upward and backward. It is not associated as are other fibroblastomas, with a hyperostosis, nor will the roentgenogram reveal any enlargement of the sella turcica

Obviously when the lesion is not promptly recognized—and years may elapse before the tumor is exposed at operation or discovered at autopsy—the tumor may be sufficiently large to cause neighborhood symptoms and changes in the sella turcica The latter may become eroded there may be uncinate attacks convulsion evidence of hypophyseal dysfunction and of hypothalamic damage In a patient referred to by Holmes and Sargent 11 years after beginning impairment of vision included in the picture were drowsiness, adiposity increased sugar tolerance headaches, dizziness, and vomiting, and the patient was completely blind One patient of our series (Case 15) had for 2 years complained of drowsiness so intense that it was difficult for her to keep awake In another (File No 11447) there was definite evidence of hypophyseal dysfunction In cases of more recent development (Case 14) there may be not the slightest evidence of an intracranial tumor

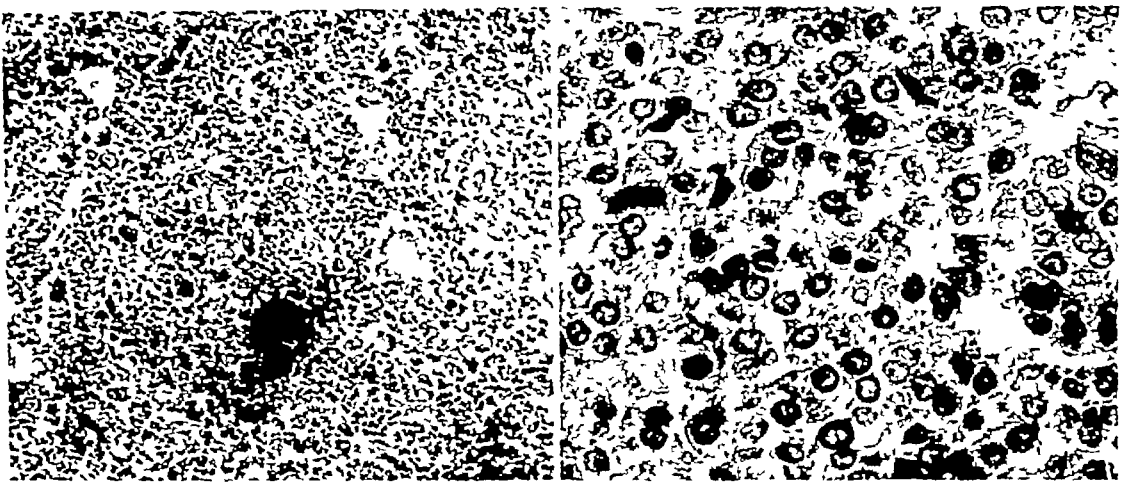

Fig 62 A suprasellar adenoma showing tendency to columnar and acinar arrangement The large chromophobic cells are seen in the high power

superior nasal field Originally there was, no doubt, a bitemporal hemianopsia His vision first became impaired in the left eye but only 6 months ago did the right eye become involved, and not until he could not sight with his right eye, in shooting did he become concerned and alarmed Occasionally he saw double, one object above the other, and occasionally too flashes of a white light in his temporal fields

Examination His blood pressure was 178/110 and his weight now and for the past 15 years 200 pounds There were no hypophyseal stigmas His vision in right eye was 6/22 and in left eye 1/60 The roentgenogram revealed almost complete destruction of the posterior clinoid processes without any depression of the sellar floor (Fig 61)

Operation Transfrontal craniotomy, right Local anesthesia In approaching the lesion the right olfactory nerve was divided The right optic nerve and chiasm were freed from the capsule before it was incised. The contents, both solid and cystic, were evacuated

Pathological diagnosis Adenoma

Postoperative course At the time of the operation the patient was practically blind in the left eye, his vision in the right eye 6/22 When last seen 10 years after the operation there had been neither loss nor improvement in vision The vision of the right eye was still 6/22 and his temporal field was still encroached upon

Structurally the suprasellar adenoma differs in no respect from the intrasellar, these tumors may be both chromophobe and chromophile, wholly solid or as in the case just cited, partly cystic (Fig 62)

In one instance in our series, a chromophobe adenoma, the tumor was of unusual dimensions, wholly without the sella, occupying the entire space between both temporal lobes, it compressed the floor of the third ventricle and contiguous structures (Fig 63)

As with intrasellar adenoma there may or there may not be associated hypophyseal symptoms In one case there was none Of the others, in one (File No 20497) amenorrhea

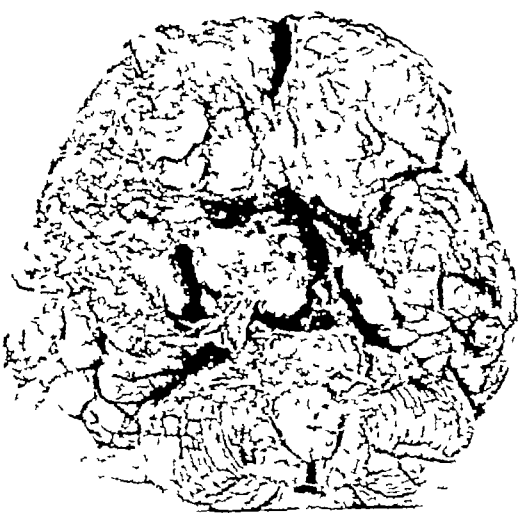

Fig 63 A large suprasellar adenoma can be seen filling the area between both frontal lobes, and compressing the base of the brain

Fig 64 Incision for transfrontal explorations

Fig 65 Suprasellar fibroblastoma Coronal incision

was a significant symptom, in another (File No 28058) acromegaly

As with the suprasellar fibroblastoma, the sella turcica is not enlarged though the clinoid processes and dorsum sellæ may in part or altogether have atrophied Should an encephalogram be made one s attention might be directed to a suprasellar lesion by the inability to visualize the cisterna chiasmatis

Although the purport of this lecture is to present and define both from the pathological and clinical aspects the so called parasellar lesions, a word might be said about the method of exposure In most instances we use what is called the transfrontal approach. Our technique for the procedure has been modified in many particulars in past years, but finally we have adopted the plan of making the scalp flap and the bone flap independently From the standpoint of the cosmetic effect, we have found two incisions most acceptable One begins 2 or 3 centimeters below the hair line in the midforehead and terminates just above the ear (Fig 64) Thus, a unilateral flap right or left as the case may be, is reflected and the incision is mostly within the hair line More recently we have used with great satisfaction and especially if the lesion be bilateral what we have chosen to call the "coronal" incision (Fig 65) This incision extends from the tip of one ear to the other and as it is wholly within the hair line the cosmetic effects are perfect

SUMMARY

Thus have been presented these eight parasellar lesions differing from one another as to their nature and origin, as to their diagnosis and prognosis, and as to their treatment.

I *Intracranial aneurisms* From the circle of Willis come more than half of the intracranial aneurisms The clinical history is more than suggestive, almost unmistakable, but only when there has been leakage. The sudden and intense headache with rigidity of the neck muscles, with fainting or unconsciousness in the presence of bloody cerebrospinal fluid, should always arouse one s suspicion. Of the focal symptoms, oculomotor paralysis and trigeminal pain in the ophthalmic division are the most constant. Periods of remission of weeks and months duration, suffice to differentiate this parasellar lesion from tumor

II. *Tumors of the optic nerve and chiasm* Globular tumors, almost always gliomas, are found occasionally involving one or both optic nerves alone or with the chiasm Mostly seen in children the diagnosis is speculative unless by the roentgenogram one finds the optic foramina enlarged and the anterior section of the sella turcica expanded forward Primary optic atrophy and field defects are inevitably associated with loss of visual acuity They do not lend themselves to surgical treatment.

III *Tumors of the lesser wing of the sphenoid* Since the number of arachnoid villi from which the fibroblastoma takes its origin are more numerous in the base of the skull this tumor is most frequently found in the

sellar and parasellar regions One of the sites of predilection is the lesser wing of the sphenoid, variable in size, sometimes crawling forward over the anterior fossa, sometimes backward into the middle fossa Definitely unilateral, their recognition will not be difficult when primary optic atrophy homonymous field defects, with or without oculomotor paralysis are associated with unilateral structural alterations in the bony anatomy of the sella turcica as depicted in the roentgenogram There may be neighborhood symptoms disturbance of the sense of taste hypophyseal stigmas occasionally paralyses and reflex symptoms due to pressure on the middle and anterior cerebral arteries

IV *Pseudotumors*, a term introduced by Nonne to designate a circumscribed collection of fluid, synonymously spoken of as meningitis circumscripta, arachnoiditis, are seen occasionally in the suprasellar region Except possibly by the pneumogram, which may portray a filling defect of the cisterna chiasmatis the verification of this lesion is not made until exposed on the operating table With a bitemporal heminanopsia, with some enlargement of the sella turcica, primary optic atrophy and signs of hypophyseal dysfunction, pseudotumors may so mimic a solid tumor of hypophyseal origin as to be indistinguishable before exposure by operation The results of surgical treatment are surprisingly good

V *Tumors of Rathke's cleft* The term Rathke pouch tumor is a misnomer and has been loosely used to include most congenital tumors in this region The tumors under consideration do not arise from Rathke's pouch which, in the process of evolution from an invagination of the buccal cavity, becomes the anterior lobe of the hypophysis They arise from Rathke's cleft Essential to the diagnosis of these tumors is a layer of ciliated epithelium on the wall of the cyst Rather than being relatively common, as one might judge from the literature, these tumors we believe are indeed rare if our proposals as to their identification be accepted Mostly in the adult, usually cystic, sometimes within and sometimes without the sella turcica, one cannot with any degree of certainty establish the diagnosis before tissue has been removed at operation for histological study The tumor is readily dealt with by the surgeon and the end-results may be excellent

VI *Hypophyseal stalk tumors* The term craniopharyngioma should be disbarred from the nomenclature as indicating tumors that take their origin from the anatomical remnant of the original communication with the buccal cavity These tumors have nothing to do with the pharynx hence the term craniopharyngioma is altogether inappropriate In substitution we introduce the term "hypophyseal stalk tumors" a term with a correct anatomical implication The stalk tumor may originate from one of two epithelial anlagen an upper and lower nest of cells If from the upper nest they soon encroach upon the third ventricle with the usual consequences of an obstructive hydrocephalus headache vomiting papilledema, if from the lower nest pressure on the chiasm, primary optic atrophy, structural alterations about the sella turcica result With a histological picture in which a basilar layer of ameloblastic cells is a characteristic feature the stalk tumor affects the child and the adolescent, is prone to undergo cystic degeneration, with numerous areas of calcification In the differential diagnosis one must have in mind another congenital tumor, the teratoma

VII *The suprasellar fibroblastoma* In its microscopic picture similar to fibroblastomas elsewhere one must distinguish the fibroblastoma that springs from the tuberculum sellæ, the suprasellar fibroblastoma, from those which spring from the olfactory groove or the sphenoidal ridge Insidious in onset slow in growth primary optic atrophy with progressive loss of vision until blindness ensues may be the only distinguishing features

VIII *The suprasellar adenoma* Comparable in its histological structure in every particular to the intrasellar hypophyseal adenoma occasionally the adenoma of the hypophysis may grow wholly without the confines of the sella turcica, hence designated suprasellar Lacking the ballooning of the sella turcica, the inevitable accompaniment of the common intrasellar adenoma, the suprasellar or extrasellar adenoma cannot be identified before operation from any other lesion of comparable size and

of a common site The congenital stalk tumors are more common in children the adenoma after the twentieth year and the fibroblastoma after the thirtieth year

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REGENERATION OF THE SEMILUNAR CARTILAGE

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THE normal knee joint function one generally observes following semilunar cartilage extirpation still arouses some curiosity Is it because the meniscus is an unnecessary anatomical structure or does regeneration of the extirpated cartilage occur? Sir Robert Jones in replying to the question What takes the place of the cartilage made the following statement "In cases that have come to me with the history of removal of a cartilage I have found no trace of any new structure even 10 years after operation"

A G Timbrell Fisher states "The author (Fisher) has operated upon several cases for recurrence of symptoms after operation 'elsewhere,' and has never seen any evidence of regeneration of cartilage sufficient to bring about recurrence of symptoms"

Other authors, on the contrary, have reported instances of what they considered regeneration For example Mandl reports 3 patients who had had a partial extirpation of the internal semilunar cartilage Because of persistence of symptoms two of these joints were reopened 6 and 8 months later, and the extirpated portion was found to have regenerated The third patient died of intestinal carcinoma 3 years after the knee joint operation Postmortem examination showed a complete regeneration of the resected portion

Moeller cites the case of a 20 year old man whose medial meniscus was excised in 1925 Four years later the knee again locked and was reopened There was found a flat "meniscus-like" piece of tissue which was firmly fixed anteriorly and posteriorly where the normal meniscus is attached but loose in its midportion This tissue was excised and on microscopic examination was found to be connective tissue

Gibson relates a case in which a patient was operated upon by another surgeon for symptoms of internal derangement of the knee, and, as the symptoms recurred, Gibson again operated and found the internal semilunar cartilage *in situ* He assumed that the cartilage had been extirpated at the original operation and had regenerated

This problem has also been attacked from the experimental side Pfab (8) extirpated

Fig 1

Fig 2

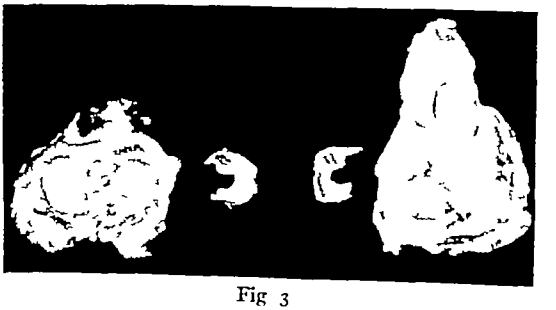

Fig 3

Fig 1 Dog 1, 14 weeks after operation Left Note complete semilunar disc of glistening white tissue replacing extirpated cartilage of left knee Note marked synovitis, complete disc of tissue replacing extirpated cartilage of right knee

Fig 2 Dog 2 Left, Complete semilunar disc of glistening white tissue, granular degeneration of articular cartilage (medial condyle) of left knee Note somewhat better replacement, less articular cartilage degeneration of right knee

Fig 3 Dog 3 Left Note narrow band of tissue replacing semilunar disc, also granular degeneration of articular cartilage of left knee Right knee same as left

Fig. 4. Photomicrograph through medial edge of tissue replacing extirpated semilunar cartilage. Dog 3 (right side). Note cells suggesting cartilage.

Fig. 5. Dog 4. Left. Note replacement following extirpation of anterior one fourth of the cartilage of left knee (8 weeks). Replacement of excised section of cartilage of right knee.

the semilunar cartilage of three sheep's knees. Six months later the synovial membranes were thickened and through their proliferation a new tissue much like a meniscus was formed. The same author (9) working with rabbits extirpated one meniscus, both menisci and in some instances the menisci plus the cruciates. In 3 cases, there was a slight tendency for the semilunar cartilage to be regenerated, in 3 others no regeneration occurred, and in another instance there was a fair regeneration.

Gibson operated upon 2 dogs doing a partial extirpation of the internal semilunar cartilage. Five months later one of the joints showed an apparent complete restitution of the extirpated portion.

Fig. 6. Dog 4. Abrupt transition from fibrocartilage (left) to connective tissue (right) which apparently does not originate from the fibrocartilage.

Fig. 7. Dog 4. Further lateral to show connective tissue sweeping in from peripheral attachment of the disc (1) and not arising from the fibrocartilaginous stump.

Dieterich extirpated small portions of the semilunar cartilages (dogs) and found the defects filled in with a "tendon-like" tissue, which contained no cartilage. Associated with this in most instances was a severe proliferating synovitis

Fiorni extirpated the external semilunar cartilages from the knee joints of 14 rabbits The joints were immobilized for 20 days following operation The joints were examined at varying periods of time and in many instances the extirpated cartilages had been replaced by connective tissue

Counting Gibson's case, there are reported in the literature at least 5 cases of regeneration of an extirpated semilunar cartilage Laboratory experiments up to this time have shown a replacement by connective tissue, rather than a true fibrocartilaginous regeneration

The object of this paper is to report our experimental work on this subject

EXPERIMENTS

The dogs will be considered individually in the order in which they were operated upon All dogs used were adults

Dog 1 On January 7, 1935, a subtotal excision of the internal semilunar cartilage of the left knee was performed, a short curved incision being employed On the right side about one-half of the cartilage was removed. A cast was applied to the left leg which was removed on the eleventh postoperative day A few days after the operation the function of the limbs appeared normal. Fourteen weeks after operation the dog was killed and the knees opened (Fig 1) On the left side the joint interior appears normal There is a complete regeneration of a circle of glistening white tissue the morphology of which is not unlike that of a real semilunar cartilage There is a slight granular degeneration of the articular hyaline cartilage

On the right side there is a marked synovitis with considerable clear, synovial fluid in the joint The external semilunar cartilage has lost its luster, is striated longitudinally, and is degenerating In spite of this marked synovitis, there is a replacement of the internal cartilage by a complete semicircle of non-glistening tissue There is here also a granular degeneration of the articular cartilage

Microscopic study of the new-formed tissue (left side) shows a compact connective tissue but no cartilage cells

Dog 2 On January 8, 1935, both internal semilunar cartilages were excised *in toto* and on the left leg a cast was applied This had to be removed in 3 days' time because of swelling and apparent discomfort

On March 26, 1935, 11 weeks later, the dog was sacrificed and the knee joints opened There was no increased synovial fluid, no synovitis

On the left side (Fig 2), there was a complete semicircle of a narrow band of glistening white tissue which grossly appeared exactly like the opposite semilunar cartilage It was considerably narrower than the extirpated cartilage Posteriorly it was well attached to the posterior cruciate ligament, anteriorly to the transverse ligament and laterally to the synovial membrane There was granular degeneration of the articular hyaline cartilage

On the right side regeneration had taken place to an even greater extent

Microscopic sections made through the apparently regenerated cartilage revealed a compact fibrous tissue but no evidence of cartilage Section through the articular cartilage showed fraying and degeneration of its superficial surface

Dog 3 On January 11, 1935, a bilateral complete extirpation was done, a cast being applied to the left leg In 1 week's time the cast was removed

On April 18, 1935, (14 weeks) the dog was killed and the joints opened On the left side (Fig 3) there was a very mild synovitis with slightly increased fluid in the joint On both sides there was a complete, but very narrow, horseshoe of regenerated tissue which looked like fibrocartilage Both sides showed hyaline cartilage degeneration on the lateral condyles

Sections cut transversely through the regenerated tissue on the right side showed a well developed connective tissue In places, however, one could make out slightly bluish areas suggesting cartilaginous matrix and in other places a few cells which looked like cartilage (Fig 4)

Dog 4 On January 21, 1935, the anterior one-fourth of the left internal semilunar was excised and on the right side a cuneiform section, measuring 4 millimeters externally, was removed just anterior to the internal lateral ligament No fixation was employed.

On March 22, 1935, (8 weeks) the dog was killed and the joints opened Grossly the joints appeared practically normal On the left there appeared to be a complete regeneration of the anterior one-fourth of the fibrocartilage, and on the right side the gap was filled in with a tissue which was grossly fibrocartilage

Sections at the junction of the fibrocartilage (Fig 6) with the newly regenerated tissue showed an abrupt transition from fibrocartilage to connective tissue The new tissue consisted entirely of connective tissue, there being no cartilage cells present It apparently originated entirely from the connective tissue of the synovial membrane laterally (Fig 7), since there was no evidence that connective tissue was growing out from the fibrocartilaginous stumps

SUMMARY

A complete extirpation of the internal semilunar cartilage was done on 4 knee joints subtotal extirpation on 2 and partial excision on 2 others. In 3 cases the joints were immobilized for 11 7 and 3 days time The joints were reopened 8 to 14 weeks later In every case the extirpated cartilage was replaced by a semilunar disc of firm glistening tissue which grossly was similar in every way to true fibrocartilage. Microscopically this was found to be connective tissue. In 1 case *a few cells, suspiciously like cartilage, were* seen

Granular degeneration of the articular cartilages of the medial tibial and femoral condyles was a uniform finding in each of these experimental cases.

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AMNIOTIC FLUID CONCENTRATE AS AN ACTIVATOR OF PERITONEAL IMMUNITY[1]

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A CONSIDERABLE and sustained mortality and morbidity from postoperative peritonitis brings forcibly to our attention the inadequacy of established methods in dealing with this problem Notwithstanding the high degree of perfection attained in our aseptic and antiseptic technique we are still confronted by the specter of infection following surgery of the serous cavities

In our attempt to meet this situation we find a very promising possibility in immunization of the peritoneal cavity by the operative or pre-operative introduction of a stimulating agent

It is now definitely established, both clinically and on experimental animals, that the introduction of certain foreign substances into the peritoneal cavity will excite the production of a defense exudate The contents and volume of this exudate will be determined to a large degree by the character and amount of the substance introduced Generally, this exudate may be said to contain serum, leucocytes, erythrocytes, fibrin, lytic ferments, opsonins, and other antibodies, and, presumably, a host of unknown substances which influence the processes of defense and repair However, such activation of the peritoneal defense mechanism should not be attained at the risk of destructive irritation A stimulation threshold exists beyond which one cannot go without causing tissue damage The level of this threshold shows a wide individual variability and may be observed in the experimental animal and in operative procedures on human patients who have received pre-operative instillation of a stimulating agent (16) Where the optimum reaction to the activating agent does not exceed the level of the stimulation threshold, the exudate is usually pink in color, slightly murky, and contains considerable fibrin The differential exudate white cell count will be preponderantly neutrophilic and the sediment will show comparatively few erythrocytes or mesothelial cells (Fig 1) If the level of the threshold is exceeded we see reaction in proportion to the excess In these latter cases the exudate is hemorrhagic, the primary neutrophilic preponderance, common to most acute peritoneal exudates, is soon replaced by the large, wandering cells (so called histocytes) and the exudate sediment shows an abundance of erythrocytes and cell detritus The systemic reaction serves as a further guide in determining the irritating effect of a given agent This may vary from no reaction at all, as in the case of innocuous substances, up to a severe local and systemic disturbance in the use of the more active irritants In these latter cases intraperitoneal injection is followed by local pain, tenderness, and a varying amount of abdominal distention, fever, malaise, anorexia, and the upset of body chemistry common to such reactions

The history of abdominal surgery is replete with attempts to modify or prevent postoperative adhesions, but comparatively little attempt has been made to establish a harmless, reliable method of peritoneal immunization, in fact there are only two agents in common use for this purpose (6, 10, 13)

Substances proposed for the prevention of postoperative adhesions would concern us little in this paper were it not for the danger attendant upon their use The greatest risk lies in their introduction in cases likely to develop postoperative infection Such agents as papain (8) or pepsin (15) which are said to accomplish the prevention of peritoneal adhesions through the digestion of fibrin are admittedly destroying a first line of defense, fibrin being a most important element in the peritoneal defense mechanism through its part in localizing infection and preventing absorption of bacteria and their toxins (4) Other

[1]Read at the Faulkner Hospital, Boston, Massachusetts before the Clinical Congress of the American College of Surgeons, October 18 1934

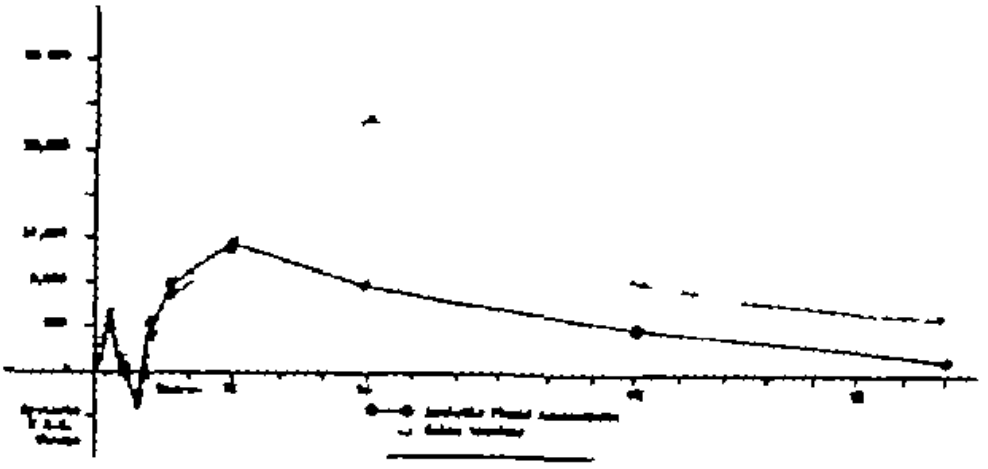

Chart 1.

agents such as hypertonic glucose (1) and sodium ricinoleate (11) which call forth the production of a tremendous peritoneal transudate are a distinct menace in the presence of postoperative infection, since they too defeat the all important process of localization In the case of sodium ricinoleate there is also widespread cell disruption (Fig 28)

The elements of defense and repair contained in the peritoneal exudate bear a normal relation to each other in their defense activities (9) This interdependence is of the utmost importance in carrying out the whole process of immunity and repair Any agent which upsets this normal order of action by stimulating one part of the defense mechanism at the expense of another or by destroying one or more parts of the whole, is obviously detrimental and its use is difficult to justify

As a harmless but effective activator of peritoneal immunity we use a purified concentrated, bovine amniotic fluid (7) In our early work with amniotic fluid our efforts had to be confined to cases of abdominal cesarean section since these were the only operations at which a supply of the fluid in a reasonably sterile condition was available In a small series of cases, over a period of 4½ years, the results were so satisfactory as to justify the use of this agent in abdominal operations other than cesarean sections. Further to establish the efficacy of this substance as an activator of peritoneal immunity a small series of laboratory animals were used and our combined observations were published in 1927 (6)

An essential to the extended application of this new technique was the establishment of an ample and reliable source of supply of the whole fluid and a method of purification which would render the end product practically innocuous. For this purpose bovine amniotic fluid was selected By a process of concentration fractionation, and purification, certain proteins, serum albumins, lipoids, and other potentially harmful substances are removed from the whole fluid. The end product we refer to as amniotic fluid concentrate [1]

In 1929, Rankin and Bargen reported a series of clinical cases in which they used a bacterial vaccine made from cultures of colon bacillus and streptococci (10) This agent was employed for pre-operative peritoneal immunization only Steinberg and Goldblatt observed the action of this vaccine to be non specific and have modified its preparation by suspending the killed colon bacilli in a 1 per cent solution of gum tragacanth (13) Since bacterial vaccines and amniotic fluid concentrate are the only two agents in common use as activators of peritoneal immunity their respective merits will be referred to in some detail.

A total of 70 dogs were used in an experimental study of the basic principles of peritoneal immunization The local and systemic effects of amniotic fluid concentrate and colon bacillus vaccine when introduced into the peritoneal cavity were checked by the use of

Grateful acknowledgment is made to the Eli Lilly Company for their valuable assistance in the preparation of amniotic fluid concentrate and for an abundant supply of this product for clinical and laboratory trial

TABLE I.—SUMMARY OF PERITONEAL REACTION IN 40 NON-INFECTED CASES

Substance	Average systemic W B C. optimum rise	Time to optimum reaction	Character of exudate	Average exudate W B C	Fibrin	Peritoneum	Clinical course following injection
Amniotic fluid concentrate	12 000	6–12 hours	Clear, thick blood tinged	75 000	High	Pink, smooth injected	Mild reaction no apparent discomfort
Colon vaccine	24,800	48–72 hours	Bloody murky, dark	120,000	Very slight	Hemorrhagic, markedly injected	Uncomfortable for 24 to 48 hours Often severe reaction
Control—normal saline	8,000	6–12 hours	Thin, blood tinged	15 000	None	Pink, moderately injected	Mild reaction, no apparent discomfort
Merthiolate and normal saline	12,000	6–12 hours	Thin, blood tinged	22,000	None	Pink, moderately injected	Mild reaction, no apparent discomfort

control substances, such as normal saline, papain, merthiolate in normal saline, and sodium ricinoleate The animals were divided into two main groups, infected and non-infected Taking the non-infected group first we noted the systemic and local reaction to colon vaccine, amniotic fluid concentrate, normal saline, and merthiolate (1 20,000) in normal saline In a small number of animals we tried added control checks with papain and sodium ricinoleate In the infected group we used colon vaccine, amniotic fluid concentrate, merthiolate in normal saline, papain, and further controlled the experiments by the use of untreated animals Observations on both groups were made through the medium of systemic and exudate white counts (total and differential), fibrin content of the exudate as determined by clotting, peritoneal sections and smears, cultures, and the clinical course of the animals With suitable allowance for the wide individual variability common to dogs, and for the difficulty of maintaining a standard of virulence in the bacteria used, we were able to make some fairly consistent findings over the entire group

Our first observation was the immediate clinical reaction of the animal to the agent used In the case of the amniotic fluid, normal saline, and merthiolate animals no immediate or remote discomfort was noted These dogs were practically as well at any interval following the intraperitoneal injection of these substances as before their use The animal receiving sodium ricinoleate gave evidence of great pain during the process of injection and was sick and very uncomfortable until sacrificed at 12 hours In the dogs receiving colon bacillus vaccine, a rather severe local and systemic reaction was noted They seemed to be in considerable distress as evidenced by whining, restlessness, anorexia, and malaise There was also noted varying degrees of abdominal distention This condition lasted usually from 24 to 48 hours One dog was in such pain immediately following the introduction of the colon vaccine preparation that the use of morphine was necessary Three of these uninfected colon vaccine dogs died before the usual 48 hour immunization interval had elapsed and autopsy failed to reveal the cause of death Cultures of the vaccine used were negative

Our next observation was the systemic white count (Chart 1) These tests were made when the dog was received, previous to any medication or manipulation, and again at the time of each peritoneal inspection. In the infected animal, it was made before the introduction of living bacteria and at the time of the postmortem examination, whether the animal died or was sacrificed

In both the infected and non-infected group, the systemic white count was much higher in the colon dogs than in the amniotic or control dogs The slight initial rise and fall was fairly constant in all animals and probably marked the stage of sudden withdrawal of leucocytes from the blood stream to meet a local emergency Dogs receiving amniotic fluid concentrate reached the peak of their systemic white count at 12 hours, while colon vaccine animals continued to rise for 24 hours In each case gradual recession followed until at the end of 72 hours the count in the colon animals exceeded that of the amniotic fluid concentrate animals by about 25 per cent (Table I)

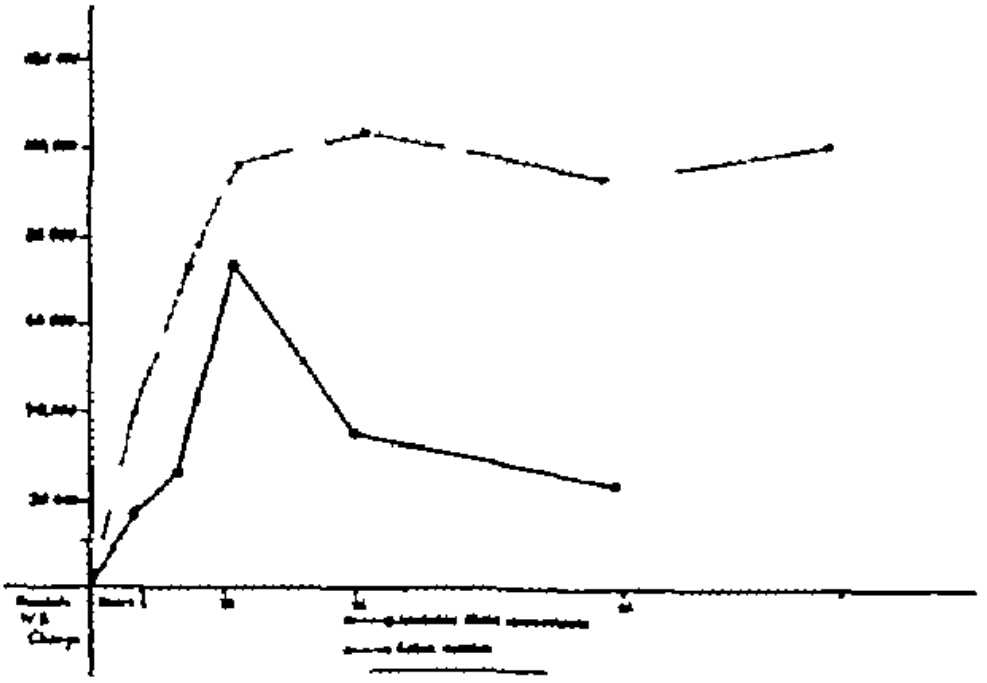

Chart 2

When the peritoneum was opened we observed the amount and character of the exudate. Color consistency white cell count (total and differential) clotting and cell detritus were the main points checked in making the comparison. The condition of the peritoneum was noted grossly and sections were taken for microscopic examination

All exudates showed a degree of redness ranging from a light pink, in the animals in which amniotic fluid and saline were used to a heavy blood red in the dogs in which the colon vaccine was used The consistency of the exudate was largely dependent on the fibrin content. This was determined roughly by the amount and speed of jelling In every instance the peritoneal exudate in the amniotic fluid animal jelled solidly in from 3 to 5 minutes and in 1 dog, 4 hours after the introduction of amniotic fluid concentrate, the exudate jelled in the stem of a large syringe within the abdominal cavity The differential white cell count of the exudate in all animals was characterized by an early preponderance of neutrophilic leucocytes Following this primary reaction to the stimulating substance the neutrophilic leucocyte count receded and the larger phagocytic cells, so called histocytes, invaded the field in increasing numbers The animals receiving colon vaccine gave the highest average total white cell count (Chart 2) Taking this exudate white cell count as a guide we observed that the optimum reaction in the colon series occurred at approximately 24 hours and was sustained for 48 to 72 hours At about the 24 hour period there was a definite recession of the neutrophiles and a tremendous increase in the histocytes (Figs 17 18 and 19) In the amniotic concentrate animals, optimum reaction was obtained in approximately 12 hours and was followed by an immediate recession of the total white cell count if infection or further stimulation were not introduced A relatively small number of histocytes was noted If the number of exudate white cells induced by a given agent were an index of the animal s immunity when infec

TABLE II —INFECTED CASES—27 DOGS

	No	Per cent
Lived	8	70
Died	9	30
Amniotic fluid concentrate—8		
Lived	7	87 5
Died	1	12 5
Colon vaccine—9		
Lived	6	66 6
Died	3	33 3
Controls—8		
Lived	5	62 5
Died	3	37 5
Merthiolate and normal saline—		
Lived	1	50
Died	1	50

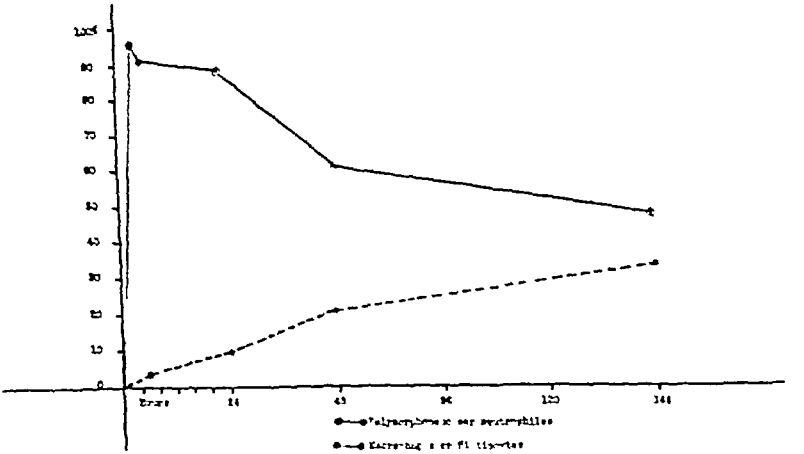

Chart 3

tion was superimposed, it would serve as a strong recommendation for the use of the selected agent Such, however, is not the case In fact, the percentage of recoveries of infected animals protected by amniotic fluid concentrate was higher than in the case of animals protected by any other substance (14) (Table II) In the control animals treated with normal saline and merthiolate in normal saline, the exudate white count averaged 15,000 to 20,000, respectively (Fig 3) The protection in these animals was very transient

In normal, untreated dogs we found no exudate and no peritoneal white counts Smears of the normal peritoneum showed an abundance of healthy mesothelial cells (Fig 4) The complete absence of other cellular structures is interesting in view of the fact that Dickson and Rixford claim a normal intraperitoneal white count of 23,000 per cubic millimeter in the human with histocytes forming 45 per cent of the total When we consider that the human cases from which these deductions were drawn were sufficiently pathological to require surgical intervention, it may account, in part at least, for the discrepancy between the human cases and our laboratory animals These investigators further suggest that the preponderance of histocytes found in the exudate of cases receiving colon vaccine, 48 to 72 hours before operation, are the most effective part of the defense mechanism and the beneficial effect derived from the use of colon vaccine, before operation, is due to their activity This is contrary to our observations

Figures submitted by Smith in his attempt to immunize rabbits by the intraperitoneal and subcutaneous injection of streptococcus antitoxin are in keeping with our own conclusions on this point A chart plotted from Smith's figures shows a rapid rise of neutrophiles in the first 2 hours to about 96 per cent of the total white cell count with gradual recession, over a period of 5 days, to about 50 per cent (Chart 3) During this period there is a gradual rise of the histocytes to about 30 per cent of the total It is our observation that histocytes are super-phagocytes and come into the picture late in response to the influence of dead tissue Smith's findings, together with our own, suggest that there is some basis for this conclusion Contrary to this usual relationship, however, it is not uncommon to see an abundance of histocytes and neutrophiles in the same field where the infection or irritation has been severe and long sustained (Fig 5) This fact alone suggests that local immunity cannot be measured in terms of the total or differential exudate white cell count Other factors, chiefly humoral, play a most important part (9)

The technique employed for superimposing infection in the vaccinated and control animals was varied In the first three series colon vaccine, amniotic fluid concentrate, normal saline solution, and untreated control dogs

were used. A method proposed by David and Loring was followed, in which the agar slant with its 24 hour culture of living bacteria was placed in the peritoneal cavity through a *small abdominal incision* In the remaining animals we used the method of Steinberg and Goldblatt introducing the living organisms in 40 cubic centimeters of a 2 5 per cent gum tragacanth solution by the use of a needle and syringe. In a single dog 50 *cubic centimeters* of an exceptionally heavy concentrate of colon vaccine (four billion per cubic centimeter) in normal saline was used for the purpose of comparing local and systemic reaction as well as the degree of immunity when infection was introduced 48 hours following vaccination (Fig 6) It was our impression that this animal did generally better than the average colon vaccine dog In a single series of 4 dogs comprising animals treated by amniotic fluid concentrate, colon vaccine, papain, and the untreated control dog 50 cubic centimeters of a virulent culture of colon bacilli and streptococci was injected intraperitoneally in each treated animal at the same time the immunizing agent was introduced. The untreated control animal received a similar amount of the infecting agent In the case of the colon vaccine animal, death followed at 12 hours the papain animal died at 15 hours and the amniotic concentrate and control animals survived the infection. The amniotic concentrate dog was quite sick for 24 hours following which improvement took place until he was sacrificed at 48 hours for the purpose of obtaining *smears* and *tissue sections*. The control dog continued very sick up to the 48 hour period at which time he also was sacrificed for comparative study This experiment was an interesting observation on the protective value of the agent used when infection was introduced at the time of peritoneal vaccination but it was not repeated because no claims are made for the protective value of colon vaccine or papain when employed in this manner

A comparative study of the peritoneal smears and sections of the infected and uninfected groups gives some idea of the physiology of the peritoneal defense mechanism and demonstrates the variations of the classical reaction that occur in response to the use of certain substances.

Standard textbook description (9) of the reaction of the peritoneum to irritation or infection depicts for us the formation of a subserous edema a choking of the vessels with leucocytes margination and migration of the white cells through the vessel walls into the surrounding tissues the escape of varying *numbers of red cells with the leucocytes* and the delivery of the subserous edema, at least in part, into the peritoneal cavity where it assists in the formation of a plastic exudate and provides a medium for the activity of the phagocytes, opsonins and other anti-bodies, lytic ferments etc. Following the successful conclusion of the defense reaction we have the terminal defense-repair effort resolution. This activity is marked by the return of neutrophilic leucocytes to the vessels a tremendous increase in the number of large wandering cells recession of the subserous edema, and a restoration of surface continuity In our attempt to activate the peritoneal defense mechanism by the use of amniotic fluid concentrate we have succeeded in reproducing this picture.

Taking a section of normal peritoneum (Figs 9 and 10) as a standard and comparing it with a section of peritoneum from a dog that had been injected *intraperitoneally* with 50 cubic centimeters of amniotic fluid concentrate 12 hours previously (Fig 11) we find that definite changes of a defensive nature have taken place. Most impressive is the tremendous edema of the subserous tissues. The lymphatics in the loose areolar tissue are notably dilated and the blood vessels show typical margination and migration of the leucocytes (Fig 12) The veins, especially are distended in keeping with the normal physiology of defense. The mesothelial layer is intact and from its relation to the subserous edema, it is not difficult to visualize this structure acting as a filter through which the defense edema is delivered into the peritoneal cavity where it forms the exudate common to peritoneal response to infection. Figures 13 and 14 show the next step in the defense mechanism when infection enters the field. The dog from which this section was taken received a virulent cul-

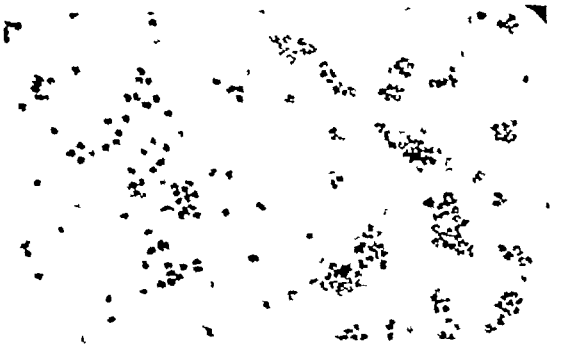

Fig 1 Fig 2

Fig 1 Smear of visceral peritoneum reaction to amfetin at 12 hours ×110

Fig 2 Smear of visceral peritoneum reaction to colon vaccine at 72 hours ×110

Fig 3 Fig 4

Fig 3 Smear of visceral peritoneum reaction to normal saline at 12 hours ×110.

Fig 4 Smear of normal visceral peritoneum of young healthy dog ×110

ture of Streptococcus hæmolyticus at the same time that amniotic fluid concentrate was introduced The dog survived the infection and was sacrificed at 48 hours to obtain specimens Most striking in the low power study of this picture (Fig 13) is the tremendous number of leucocytes present in the subserous tissue The subserous edema, noted in uninfected animals, has been largely delivered into the peritoneal cavity Here the defense elements contained in this edema, such as opsonins and other anti-bodies, lytic ferments, fibrin, certain catalytic agents, etc join in the general defense repair effort A section of fibrinous exudate (Fig 14) seen on the peritoneal surface of this animal is very instructive since it suggests the probable order of defense and resolution A mass of fibrin, literally loaded with leucocytes and a small number of histocytes, is seen as it is being lifted off the mesothelial cells by a layer of huge histocytes This picture is typical of the normal order of defense and repair and in the presence of such a vigorous defense reaction it is not difficult to understand why we find less remote postoperative adhesions in some cases suffering from a severe primary infection than in cases of peritoneal surgery in which infection has not

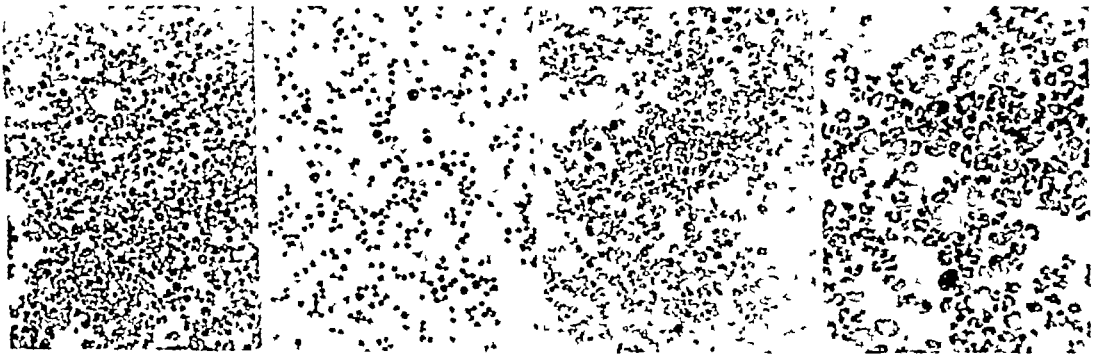

Fig 5 Fig 6 Fig 7 Fig 8

Fig 5 Smear of peritoneal exudate from control animal 60 hours after infection with colon bacillus and Streptococcus hæmolyticus ×120

Fig 6 Smear of visceral peritoneum 48 hours after injection of excessive dose of colon vaccine (4 billion per cubic centimeter) in normal saline. ×120

Fig 7 Smear of visceral peritoneum 60 hours after infection with Streptococcus hæmolyticus and colon bacillus in dog protected by amniotic fluid concentrate Immunization interval 12 hours. ×120

Fig 8 (Same as Fig 7) Oil immersion Smear taken from dog making excellent clinical recovery Note the apparent activity of the histocytes in this stage of resolution ×250

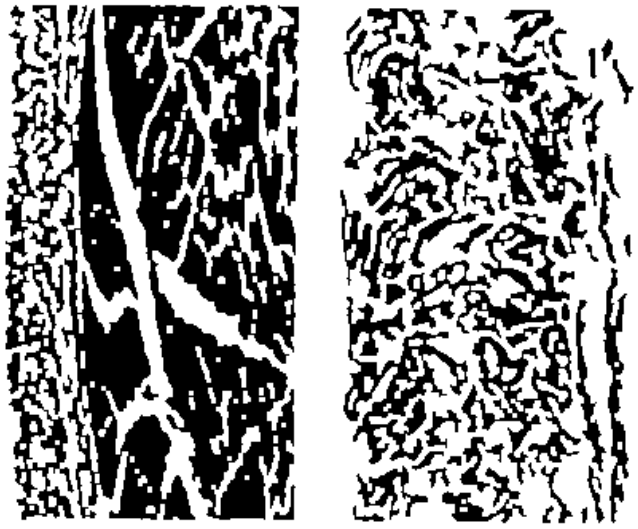

Fig 9, left Normal peritoneum—low power ×30
Fig Normal peritoneum—high power × 35

played a part Attention is also called to the fact that in this entire defense response under stimulation by amniotic fluid concentrate hemorrhage is not conspicuous

The intraperitoneal introduction of irritating chemicals foreign bodies, bacterial vaccines, or any combination of the foregoing causes a considerable variation in this defense picture Hemorrhage is present in proportion to the amount of irritation or trauma The volume of exudate or transudate is influenced markedly by the type and tonicity of the irritating substance and the exudate cell picture at the end of 24 to 72 hours may be so altered as to be almost a complete reversal of the classical order of the defense mechanism

Fig left Peritoneal reaction to stimulation by amniotic fluid concentrate t hours ×48
Fig Oil immersion of Figure to show leucocytic margination and migration ×350

Specific instances of the distortion of the peritoneal defense mechanism may be seen in the use of substances such as papain sodium ricinoleate, hypertonic glucose, various oils and the bacterial vaccines, especially if the latter be suspended in a gum tragacanth solution

Considering first the peritoneal response to the introduction of bacterial vaccines (Fig 17) we see at the end of 24 hours a marked cellular infiltration of the subserous tissues with the formation of a considerable amount of surface exudate There is also present a moderate amount of subserous edema A closer study of the field under high power and oil immersion (Figs 18 and 19) brings out the fact that the cellular infiltration is almost entirely histocytic The exudate appears to be

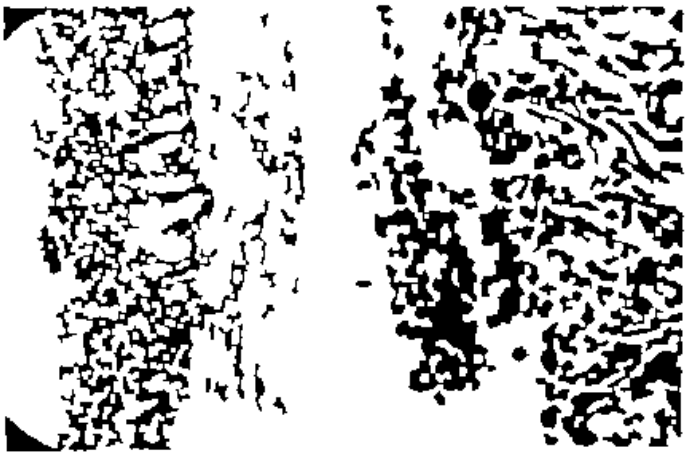

Fig 3 Fig 4

Fig 3 Peritoneal reaction to Streptococcus hemolyticus introduced at the same time as the amniotic fluid concentrate ×30
Fig 4 Oil immersion of Figure 3 to show phagocytic

Fig 5 Fig 6

activity present in the vicinity of the fibrinous exudate
Fig 5 Section of peritoneum from control animal following infection ×30
Fig 16 Same as Figure 5, oil immersion ×167

Fig 17

Fig 18

Fig 17 Peritoneal response to colon vaccine in gum tragacanth at 24 hours ×47

Fig 18 Enlargement of Figure 17, to show subendothelial infiltration of histocytes ×135

Fig 19

Fig 20

Fig 19 Oil immersion of Figure 17 to show cellular structure of exudate ×250

Fig 20 Peritoneal reaction to normal saline at 12 hours —introduced for comparison ×23

made up completely of these large wandering cells enmeshed in a few loose strands of fibrin Not only does the serous surface appear well supplied with histocytes but the immediate subserous connective tissue is literally choked with them and the infiltration even extends into the muscle layer Consistent with this cell picture is the fact that the blood vessels in this same section fail to reveal the presence of the typical defense picture of leucocytic margination and migration

The peritoneal reaction to infection at 48 hours after the introduction of a 24 hour living culture of colon bacillus on an agar slant may be seen in Figures 21 and 22 This animal had received the full 72 hour immunization interval recommended in the use of colon vaccine The subserous connective tissue shows no evidence of edema and contains areas of hemorrhage The exudate is made up almost entirely of histocytes and abundant cell detritus In view of the fact that the defense exudate in animals treated with colon vaccine is usually hemorrhagic in appearance, the presence of subserous hemorrhage and a large amount of cell detritus in the surface exudate is significant This seems to indicate that the color of the peritoneal exudate in these animals is due to broken down red cells

The overwhelming number of histocytes in

Fig 21

Fig 22

Fig 23

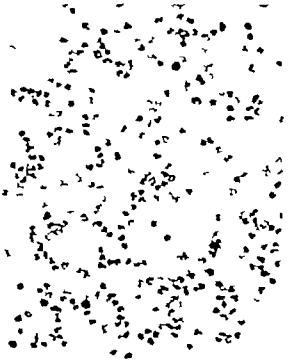

Fig 24.

Fig 21 Low power study of peritoneal response to 24 hour agar slant of colon bacillus Dog protected by 72 hour immunization interval with colon vaccine ×54.

Fig 22 Same as Figure 21—oil immersion Magnification to show hemorrhagic exudate and predominance of histocytes ×280

Fig 23 Smear of visceral peritoneum from dog protected by colon vaccine—72 hours immunization interval —sacrificed at 48 hours after infection with colon bacillus ×133

Fig 24 Smear of visceral peritoneum protected by amniotic fluid concentrate—12 hour immunization interval—sacrificed at 48 hours following infection with colon bacillus ×133

Fig 25

Fig 26

Fig 27

Fig 28

Fig 25 Peritoneal response to the introduction of papain (200,000 dilution) to show digestion of mesothelial layer and contiguous, subserous connective tissue × 15

Fig 26 Effect of sodium ricinoleate (per cent solution) on peritoneum ×22

Fig 27 Same as Figure 26—increased magnification to show disruption of cell structures ×106

Fig 28 Smear of exudate t hours from animal injected with sodium ricinoleate to show disruption of cell membranes of histocytes and low kite cell count × 10

the exudate of the infected and non infected colon vaccine animals may be explained by the presence of the dead bacteria of the vaccine and the excess of cell detritus in the exudate This view is in keeping with the established function of the histocyte as a scavenger and may be some indication of the destructive effect of a given agent.

Papain digests fibrin and the mesothelial layer of cells (Fig 25) To this extent localization of infection and the prevention or retardation of absorption of bacteria and their toxins is interfered with Sodium ricinoleate in a 1 per cent solution is extremely irritating (Figs. 26 and 27) It sets up a violent reaction in the peritoneal cavity with the formation of a tremendous transudate of low cell count (Fig 28) There is also present a widespread disruption of surface tissue cells and phagocytes. Hypertonic glucose solution (20 to 50 per cent) while not destructive like sodium ricinoleate, does induce the formation of a large transudate and consequently interferes with localization of infection resulting in a high mortality among the experimental animals (2) The oils are notorious for their ineffectiveness in preventing adhesions and for the formation of so called oil tumors

RESULTS OF STUDY

The purpose of this investigation has been to weigh the merits of substances commonly introduced into the peritoneal cavity to establish peritoneal immunity or prevent adhesions, or both Our chief concern is to secure the highest possible degree of protection against postoperative infection and adhesions with a minimum of physiological disturbance. In accomplishing this point an important factor is the time required in obtaining the optimum defense reaction to a given stimulating agent, the so called immunizing interval. Equally important is the systemic effect upon the patient Guided by previous teachings and our own experimental work we have tried to reproduce, aseptically the classical peritoneal reaction to infection

We believe that the ideal activator of peritoneal immunity is a substance which chemical analysis and extensive clinical and laboratory trial has proved innocuous one which may be used before operation without discomfort or clinical upset one which has an immunizing interval sufficiently brief to be adaptable to operative introduction one which is vigorous enough to be effective without overstepping the stimulation threshold and finally one which will induce a peritoneal reaction similar in character to that laid down by the normal peritoneum in the presence of infection In addition to these requirements such an agent should be stable and free from remote untoward reactions

From the experimental and clinical evidence upon which this paper is based it has been definitely proved that amniotic fluid concen-

trate most effectively meets the foregoing requirements The only other substance now being employed to any extent as an activator of peritoneal immunity is the bacterial vaccine of Rankin and Bargen with modifications by Steinberg and Goldblatt Extensive clinical trial and laboratory experiments have proved this agent effective However its use is confined to pre-operative administration 48 to 72 hours before the abdomen is opened and the protection afforded by its introduction is attained at the cost of a considerable physiological and clinical upset and a long immunizing interval In our experimental work, at least the product itself has not proved stable

Other substances such as normal saline, papain, and sodium ricinoleate were studied chiefly as controls and for the purpose of learning their beneficial or destructive qualities in the infected and uninfected animals

A careful study of the charts, grafts, smears, and tissue sections submitted will substantiate the foregoing observations

SUMMARY

1 Evidence deduced from a study of 70 dogs shows that certain substances when introduced into the peritoneal cavity will excite the production of a defense exudate

2 The character of the exudate will depend upon the substances introduced

3 The use of agents relying upon digestive ferments or excessive irritation interferes with the normal physiology of defense and repair

4 The brief immunization interval required in the use of amniotic fluid concentrate makes it adaptable for operative as well as pre-operative introduction

5 Amniotic fluid concentrate proved to be the most effective agent used in these experiments

6 This study is aimed to contribute to the knowledge of the basic principles of peritoneal immunization and is offered as an aid and stimulus to further investigation in this comparatively new and important field

Grateful acknowledgement is made to Dr Elliot C Cutler, professor of surgery, Harvard Medical School for his generous co-operation throughout this experimental work and to Dr Robert N Nye of the Department of Pathology, Boston City Hospital, for his advice and technical assistance in the preparation of cultures

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CLINICAL SURGERY

FROM THE MAYO CLINIC

THE REPAIR OF POSTOPERATIVE DEFECTS INVOLVING THE LIPS AND CHEEKS SECONDARY TO THE REMOVAL OF MALIGNANT TUMORS

GORDON B NEW M D F A C S AND FREDERICK A. FIGI M D F A C S ROCHESTER, MINNESOTA
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THE majority of defects about the mouth, which come under the care of the plastic surgeon are congenital or traumatic, or are the result of treatment of malignant tumors While perforation of the lips, cheeks, or jaws rarely develops following proper treatment in the early stages of malignant neoplasms of these structures, the thorough removal of extensive carcinomas in these situations not infrequently results in such defects, regardless of whether eradication is effected by surgical measures, irradiation or escharotics The use of escharotics probably accounts for a proportionately higher percentage of perforations than does surgical treatment or radiation, since the destructive process is less readily controlled It is chiefly with the postoperative group of defects and their repair that we shall deal in this discussion

The occurrence of perforation following the operative removal of a malignant neoplasm about the mouth is at times interpreted as reflecting adversely on the skill and judgment of the surgeon In the majority of instances, such interpretation is entirely unjustifiable As a matter of fact, it frequently indicates a wider knowledge and greater experience in dealing with lesions of this type than is evinced by patients who reveal only slight loss of tissue In treating localized inactive malignant lesions in this situation an element of conservatism is justifiable but extensive active growths must be removed widely regardless of the deformity produced. This frequently will necessitate sacrificing a large portion of the upper or lower lip or both, and at times, a portion of the cheeks jaws, and floor of the mouth as well Moreover in most cases of this type it is highly inadvisable to carry out reconstructive procedures until after the patient has been free of evidence of the disease for a considerable time A good deal of courage and conviction on the part of the physician is required to convince the patient of the necessity of producing such a defect and delaying its closure Not only is the patient likely to seek *treatment elsewhere but on account of the scarring* greater difficulty often is encountered in carrying out repair at a later stage than would have been met in doing an immediate closure Primary closure of wounds following the removal of advanced malignant lesions, even in cases in which there is attachment to the bone is still practiced by some surgeons More often than otherwise however such efforts lead only to disappointment as recurrence promptly ensues in a high percentage of these cases At times, the extensive sacrifice of tissue renders immediate repair a physical impossibility In other instances, the general condition of the patient is not sufficiently satisfactory to permit the operation to be prolonged

The opportune time for repair of defects about the mouth which result from the removal of malignant tumors, varies with the nature activity previous treatment situation, and extent of the lesion, and with the age and general condition of the patient Generally speaking reconstruction should be delayed somewhat longer following treatment of a squamous cell epithelioma than after treatment of a basal cell growth, and longer after the removal of a highly malignant lesion than after the removal of an inactive one. A tumor that has been treated previously especially with irradiation or one that has been cleared up with irradiation may recur much later than one that has not been treated previously or that has been removed surgically This is because malignant cells may lie dormant in the dense scar for a longer time Lesions involving bone secondarily may gradually extend along the periosteum

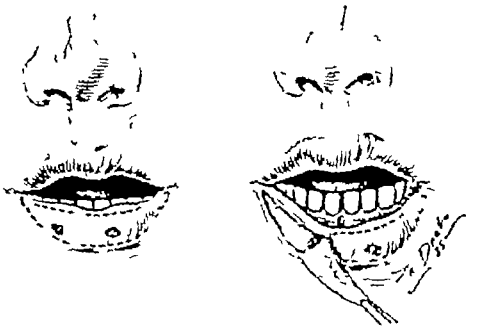

Fig 1a

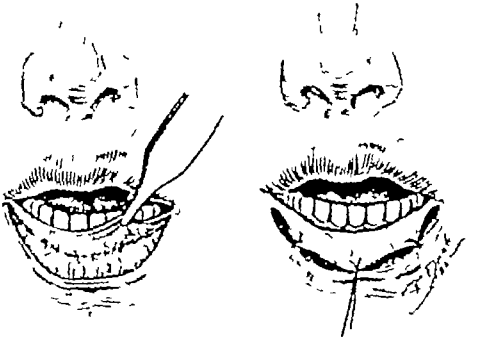

Fig 1b

Fig 1 Method of removing the mucous membrane of the entire lower lip for precancerous lesions such as thickened patches of leucoplacia, patches of keratosis, or other lesions which undergo early malignant changes Figure 1a shows the incision and a portion of the mucous membrane and subcutaneous tissue which has been elevated, in Figure 1b the mucous membrane from the inside of the lower lip has been freed rolled out and sutured to the skin

Fig 2 Completion of suturing of the mucous membrane from the inside of the lower lip to the skin

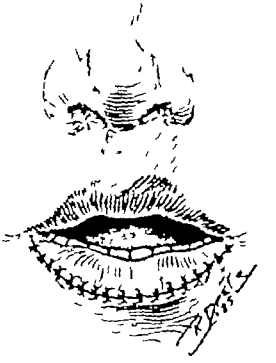

Fig 2

and recurrence become manifest much later than in the cases in which tumors affect only the soft tissues There is greater likelihood of recurrence after removal of extensive growths than there is after removal of localized tumors Malignant neoplasms that affect young individuals usually are more active and more prone to metastasize than are those which affect older people, repair, therefore, should be delayed longer in the former group than in the latter group It need scarcely be mentioned that a patient in poor general condition should not be subjected to extensive plastic repair, even though the lesion apparently has been eradicated completely Reconstruction should be delayed until the condition of the patient improves At times, the removal of a large, foul, malignant lesion of the lips or cheeks is advisable, even in the presence of inoperable metastasis, because of its deleterious effect on the general health of the patient and in consideration of those who must associate with him If the loss of tissue in such cases is too great to permit primary closure of the defect, delayed reconstruction rarely is to be considered

Most recurrences following the removal of malignant neoplasms take place within 6 months to a year Accordingly, in the cases in which elderly individuals have had tumors, which have revealed a low grade of malignancy, repair is justifiable after the patient has been well for 6 or 8 months, while with more active and extensive growths, especially in cases in which the patients are young, reconstruction is better delayed for at least a year By this time, devitalized bone will have separated, the inflammatory reaction will have subsided, and the margins of the perforation will have healed If local recurrence or metastasis is to occur, it usually, though not always, will have become evident within this period In several instances we have seen local recurrence develop more than a year after removal of a carcinoma of the lower lip and in one case both local recurrence and pulmonary metastasis became demonstrable almost a year and a half after removal of a lymphosarcoma of the cheek of an elderly individual In another case metastasis to the submental lymph nodes developed 16 years after permanent local cure of an epithelioma of the lower lip

Recurrence of a malignant growth, which develops after repair is well under way or completed, presents a serious problem Such a recurrence, which occurs beneath the graft, cannot, as a rule, be recognized until well advanced and it then necessitates sacrifice of not only the transplanted tissues but of much adjacent tissue as well Indeed, in such an event, it will be fortunate if the

Fig 3 Epitheliomas of the lower lip before and after excision of the epitheliomas

Fig 5 Extensive epitheliomas of the entire lower lip and chin and two epitheliomas of the left cheek At right, the reconstructed lower lip is shown The epitheliomas of the lip has been removed with surgical diathermy

Fig 4

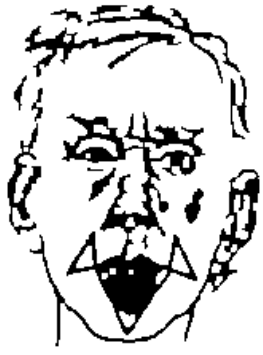

Fig 6

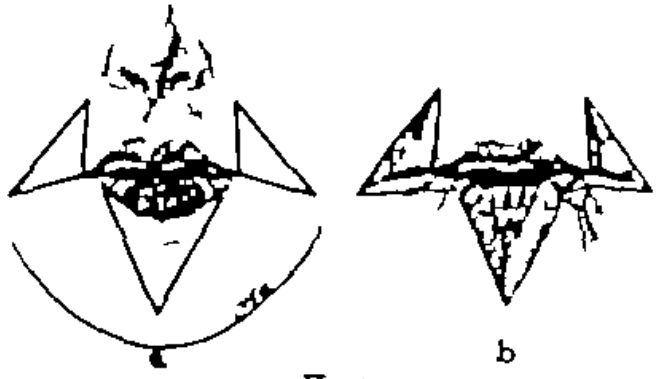

Fig 7

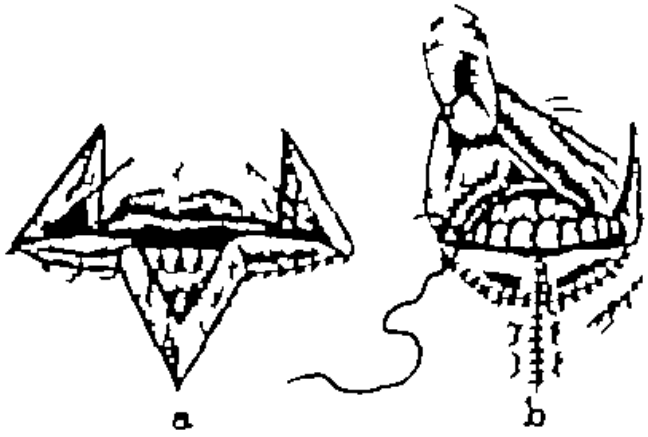

Fig 8

Fig 4 Lines of incision for excision of epitheliomas of lower lip and for plastic reconstruction of angle of mouth, order to enlarge the lip The details of this operation are shown in Figures 7 8, and 9 In certain cases the skin ing of a portion of the mucous membrane of the lip, as in Figure is combined ith this operation

Fig 6 Lines of incision for removal of the growth The details of this operation are shown in Figures 7 8, and 9

Fig 7 The lines of incision may be noted The tri angular portion removed from the upper lip and cheek does not extend through the mucous membrane into the mouth b, the small triangular area of skin, x, just anterior to the mucous membrane is excised in order to allow the freed up mucous membrane to approximate the skin, forming new vermilion margin (As far as we can make out, the technique of this operation, with the exception of few modifications, was first used by C H Mayo)

Fig 8, The dotted triangular area is excised from the mucous membrane of the inside of the upper lip on either side in order to roll in the angles of the mouth so that the vermilion margin gradually disappears at the angles, b, closure of the mucous membrane inside the upper lip ith interrupted catgut to roll in the angles of the mouth

condition has not progressed to an inoperable stage

The problem of repair following the removal of malignant lesions about the mouth varies greatly in different cases, depending on their situation, extent, and degree of malignancy Precancerous conditions, such as thickened patches of leucoplacia and keratosis, in this situation are best

Fig 10 Secondary closure following removal of the epithelioma of the lower lip This is suitable for cases in which the growths are of an active type and require cautery excision and treatment with diathermy, rather than primary plastic operation Loss of the greater part of the lower lip can be noted in left figure, as shown in right figure, the lower lip has been reconstructed with the technique illustrated in Figures 7, 8, and 9

Fig 11 Loss of greater part of the lower lip, chin, and angle of mouth, secondary to removal of extensive active epithelioma of the lip and chin. At right is shown the result of the operation The replaced portion of the lower lip may be noted

removed by superficial excision or "shaving" This consists in excising sharply an elliptical piece of mucous membrane and submucous tissue of the lip The piece, which is excised, should extend along the vermilion border of the lip and beyond the pathological tissue The posterior margin of the wound is then undercut, and the mucous membrane inside the lip is drawn out and sutured to the cutaneous anterior edge, thereby furnishing a new vermilion border for the lip If the growth appears malignant clinically, it is excised by removing a wedge from the lip, and the wound is closed primarily A high percentage of carcinomas, which originate on the lower lip, have a low grade of malignancy or are moderately active, and even though rather extensive, immediate closure of the wound is permissible following their removal Immediate reconstruction can readily be carried out, even when it has been necessary to sacrifice the entire lower lip A number of different surgical procedures have been devised for

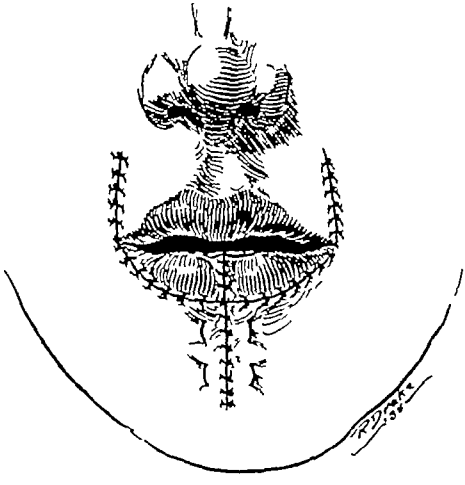

Fig 9 Completion of the reconstruction of the lower lip

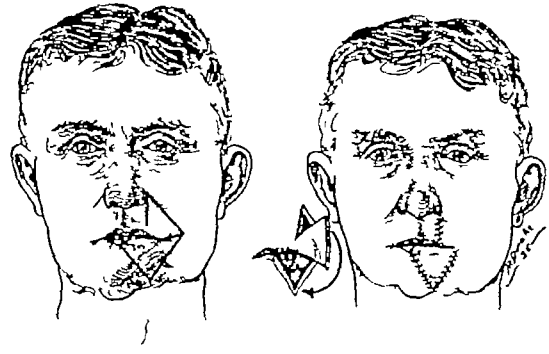

Fig 12 A flap, which has the pedicle along the vermilion margin (Estlander's operation), is elevated from the left half of the upper lip and rotated down into position along the lip, after the scarred margins have been excised As a secondary procedure, after the wounds have healed, the mouth is enlarged to the left by an incision into the angle, and by rolling out the mucous membrane. The scars which extend from the angle of the lip respectively to the ala and to the chin usually make one continuous perpendicular line

Fig 3 Loss of entire lower lip and portion of the chin, secondary to removal of an active epithelioma with cautery and diathermy View before and after reconstruction of lower lip

this purpose One of the simplest and most satisfactory of these, both as regards removal of the malignant process and the appearance and function of the reconstructed lip is excision of the growth with a wide V Following primary closure of this defect an incision should be made laterally into the cheeks, through the angle of the mouth on either side, and an inverted wedge should be removed from the inner portion of the cheeks By reversing the procedure the upper lip may be reconstructed in the same manner This is somewhat more difficult than the last procedure and the cosmetic result is less satisfactory because of the fixation of the tissues about the nose and the greater prominence of the scarring, which results from removal of a wedge from either side of the lower lip Delayed closure in such cases is, as a rule, necessary only in cases in which the growth involves the mandible or superior maxilla secondarily or when it is highly malignant.

While immediate repair is desirable in these cases it should never be carried out unless the lesion can be removed together with an adequate margin of normal tissue. This is practically im-

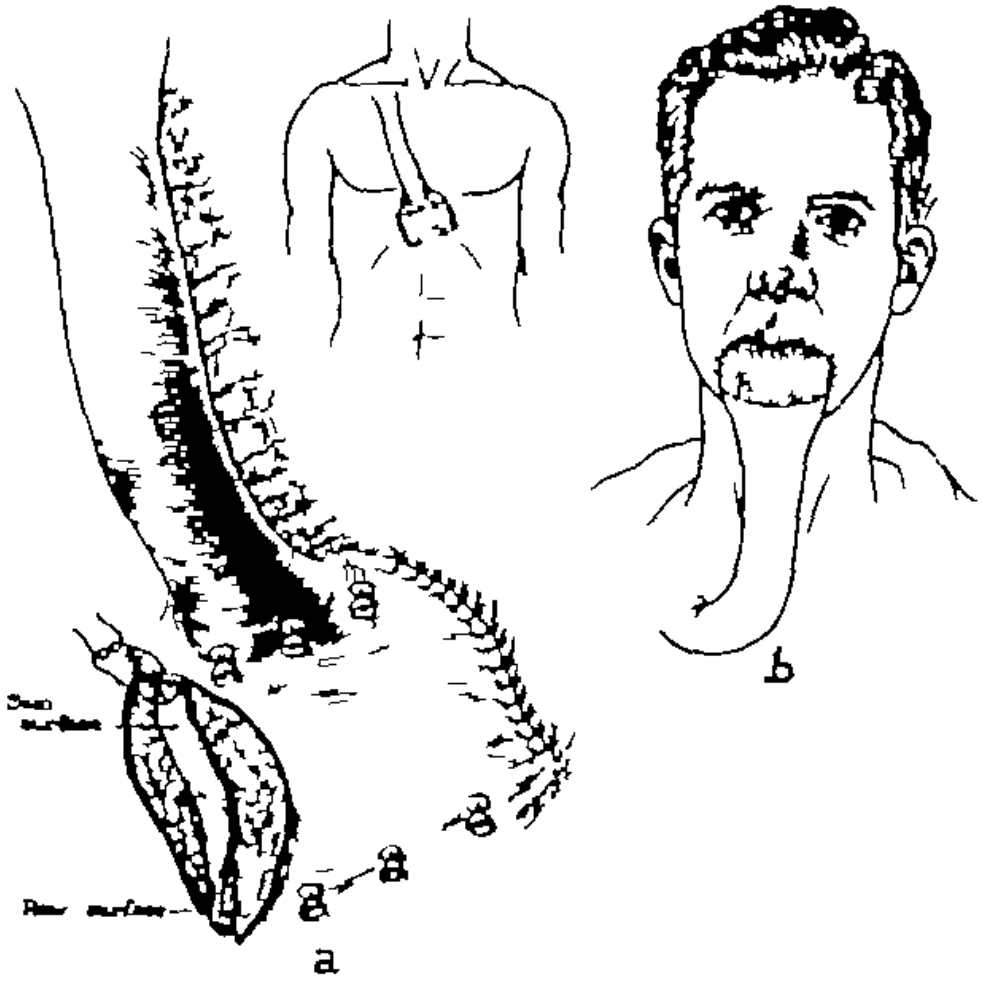

Fig 4 The flap is taked on the right side of the thorax and at second procedure the lower portion of the flap is extended and lined with full thickness skin graft, which will later form the lining of the lower lip The flap, however should not cross the midline as it does in the drawing The sutures tied over gauze above and below the outlined area hold the margins of the skin graft in position b the lined flap has been brought up and sutured in place to reconstruct the lower lip The dotted area outlines the full thickness skin graft on the under surface

Fig 15 Loss of part of lower lip, angle of the mouth, and cheek Before and after reconstruction of lower lip and closure of the cheek

Fig 17 Loss of the greater part of lower lip, cheek and angle of the mouth, with fixation of the tissues to the jaw by the scar Photographs taken before and after replacement of tissues of upper and lower lip and cheek The scarring along the lower border of the flap forming the lower lip is still to be smoothed out

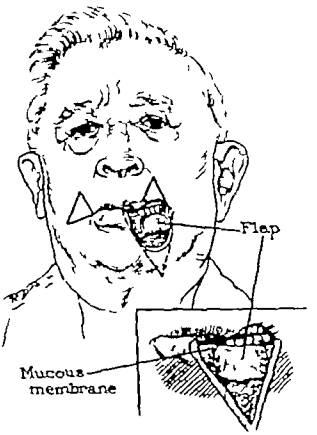

Fig 16 A flap is turned up to form the lining of the lip and sutured on either side to the mucous membrane of the lip and cheek After excising the triangles at either angle of the mouth, the skin is freed from the lip and cheek and brought together over the lining The excision of the angles of the mouth is detailed in Figures 7, 8, and 9

Fig 18 Tubed flap has been elevated and the lower end lined as illustrated in Figure 14, a It is then brought up and sutured in place to replace the lower lip and angle of the mouth. The dotted area shows the extent of the full thickness skin graft lining

possible in cases in which the carcinoma has invaded the bone There is a definite tendency when primary closure of the wound is anticipated, to excise a narrower margin of normal tissue than is consistent with safety, and the likelihood of recurrence is accordingly increased The prognosis following subsequent excision is naturally less satisfactory than it is in cases in which the primary excision has been wide, and the wound must necessarily be left open so that it is far preferable that closure of the original wound be delayed It is our practice, in cases in which wounds about the mouth are to be sutured primarily, to excise the tumor with the scalpel while in cases in which secondary closure is planned, we employ cautery excision or electrocoagulation

For some years, malignant tumors of the jaws and of the soft tissues inside the mouth have been treated in the clinic with electrocoagulation Frequently, this therapy is supplemented with the implantation of radium The wounds granulate promptly following separation of the slough and there is no interference with function, aside from slight restriction of movement of the mandible, which is the result of loss of the mucous membrane of the inside of the cheek The degree of limita-

Fig 19 Perforation of the angle of the mouth and cheek, with scarring of the upper and lower jaws, causing ankylosis secondary to removal of an epithelioma of the cheek with surgical diathermy The tubed flap on the chest may be noted, and t right, photograph of patient after closure of the perforation and correction of the ankylosis of the jaw

tion of movement varies greatly depending on the extent and situation of the scarring At times, complete ankylosis results and restoration of the lost lining is necessary for relief This is accomplished by freeing the scarred attachment to the mandible and restoring the buccal folds by relining this portion of the mouth with shaved skin grafts applied over dental compound In cases in which these lesions inside the mouth extend deeply into the soft tissues so that they lie directly beneath the skin, or are attached to it it frequently is impossible to remove them completely either with diathermy or the cutting cautery without perforating the cutaneous surface In this event provided there is not extensive involvement inside the cheek and the lesion has a low grade of malignancy, it may be possible to close the wound primarily More often however secondary closure will be advisable.

Defects that involve the angles of the mouth, the lips, and the cheeks often can be taken care of either primarily or secondarily in a single stage, with tissues from the immediate vicinity Even though the lesion has not extended deeply enough to necessitate sacrifice of the full thickness of the lip or cheek ectropion of the lip will frequently result. This can as a rule be corrected by dissecting away the scar tissue and either applying a Wolfe graft or turning in a flap from the adjacent region to cover the denuded surface. At times, when only a small perforation of the cheek is present, this can be repaired by utilizing a hinged flap from near the margin for a lining, and covering this with a full thickness skin graft.

In most cases, extensive loss will necessitate bringing in tissue from a distance for reconstruction. For this purpose pedicled flaps may be secured from the forehead neck, arm, thorax, back, or abdomen. The most favorable sites are the forehead and the thorax. While the color vascularity and texture of the tissues of the forehead render these highly desirable for the repair of such facial defects their use results in additional scarring on an exposed portion of the body If the patient is a woman, this will be, as a rule, less of a disadvantage than it will be if the patient is a man, since the skin graft used to cover the region from which the flap is taken can be very

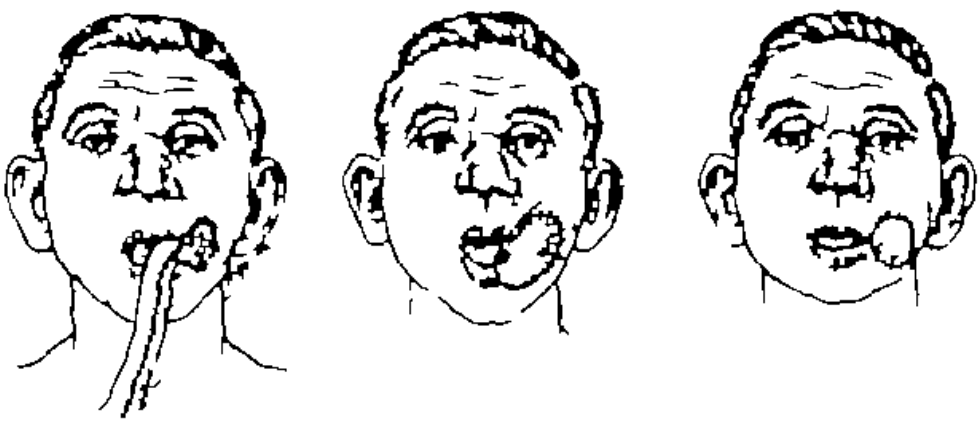

Fig 20 The first drawing shows the distal end of the tubed thoracic flap which has been elevated, opened, and carried back into the commissure between the upper and lower jaws, after the scarring has been excised to allow the patient to open the mouth The second drawing shows the tube cut across, opened up, and used as a covering for the perforation, both has been lined by the distal end of the flap The third drawing shows the completion of the plastic procedure after excision of the intervening part of the tubed flap and closure of the angle of the mouth

Fig 21 Photographs showing loss of entire upper lip and columella of the nose, following removal of an epithelioma, and after the upper lip has been reconstructed

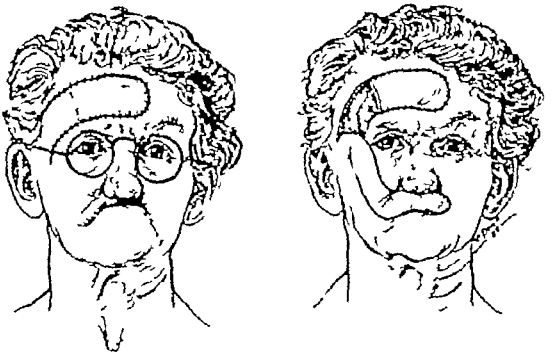

Fig 22 A delayed flap with a pedicle in the right temporal region was elevated, and the distal end of the pedicled flap, which is outlined by the dotted area, was lined with a full thickness skin graft After delay, this is brought down to reconstruct the upper lip The skin graft forms a lining for the upper lip

effectively covered with the hair If the patient has a thin skin, the scarring about the graft on the forehead becomes so inconspicuous that at times it can scarcely be noticed If the skin of the patient is thick, on the other hand, both the graft and the scar about its border may remain unduly conspicuous For this reason, flaps from the thorax or back are, as a rule, employed at the present time in the majority of cases in spite of the fact that they require considerably more time and involve greater expense to the patient because of longer hospitalization than does a flap from the forehead Whereas a flap from the forehead can be transferred and the reconstruction completed in the course of approximately 2 months, a flap from the anterior or posterior aspect of the thorax will require a much longer time Such a flap from the thorax must be tubed, which usually causes a delay of at least 3 months before transference, while a flap from the forehead is ready to be moved in approximately 2½ to 3 weeks In addition to furnishing a new skin surface, and at times, a lining as well, flaps from the thorax frequently are utilized for supplying subcutaneous adipose tissue to an area about the face Restoration of the symmetry of the two sides of the face, especially of the cheeks, is thereby possible Such a flap would, of course, not be required unless it were necessary to replace the skin as well as to supply subcutaneous fatty tissue, for otherwise, a free fat transplant would be resorted to

A lining for the reconstructed lip or cheek in these cases is furnished by grafting skin on the under surface of the distal portion of the flap Full thickness grafts are most satisfactory for this purpose The graft must be applied a sufficiently long time prior to transference of the flap to permit it to become attached firmly Flaps from the thorax must be of sufficient length to reach without tension from the point of attachment of the pedicle, which usually is situated just over or below the clavicle anteriorly or over the base of the trapezius muscle posteriorly, to the defect on the face The length of the flaps that are obtained from the region of the clavicle or from the region of the trapezius muscle is greater than the length of the flaps that are obtained from the forehead The tissues in the region of the clavicle or in the

Fig 23 Actinodermatitis of the right cheek, secondary to treatment of an angioma with radiation Three of the patches on the cheek revealed epithelioma The entire lesion was excised and replaced with a free full thickness skin graft from the inside of the arm It will be noted from the figure at right that the entire graft has taken.

Fig 24 Deformity of right cheek with loss of a portion of the malar bone and zygoma, and part of the lower jaw following removal of squamous cell epithelioma, grade 3, with surgical diathermy The deformity as corrected 3 years later with a tubed flap from the back, the fat in the tube being tailored to build out the cheek Photograph at right shows that the distortion and displacement of the ear have been corrected and the normal fullness of the cheek has been restored Further improvement could be made by forming a nasolabial fold

region of the trapezius muscle are comparatively avascular These facts explain why it requires more time to secure flaps from the latter situations than it does to secure flaps from the forehead The color and texture of grafts from the latter regions also correspond much less satisfactorily to the tissues of the face than do the color and texture of grafts which have been obtained from the forehead, but these differences become less pronounced in the course of time At times, it is of advantage to transfer the lower attachment of the chest flap to the mastoid or cervical region and then to utilize the clavicular end of the flap for the repair This may be desirable because of the thin skin in the clavicular area, or it may be necessary because the flap was not long enough

Repair of extensive loss of tissue about the mouth can be carried out very satisfactorily in many cases with local infiltration anesthesia only and at times, it is of advantage to do so This is generally true in cases in which the patients are elderly individuals As a rule however it is preferable to execute the more time-consuming and painful stages of the procedure under general anesthesia and to use local anesthesia for the minor steps and those in which the distortion incident to infiltration with novocaine will not constitute a serious disadvantage According to this scheme the original elevation and grafting of a flap from the forehead, and its transference as

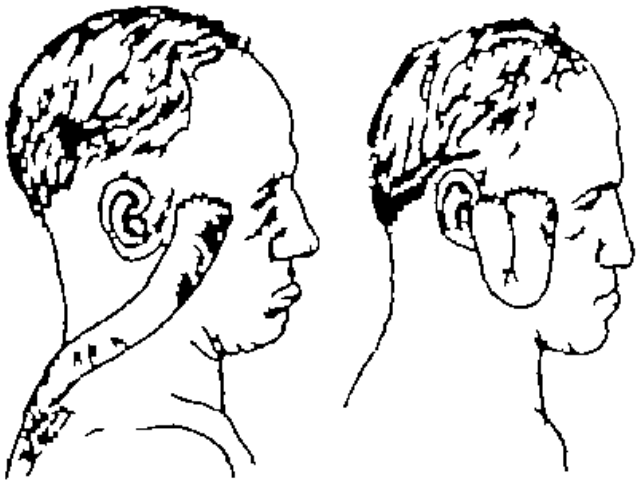

Fig 25 The distal end of the tube as carried to the upper portion of the scarred area The upper end of the tube as carried anterior to this in the temporal region and the tube was then smoothed out to replace the lost tissue of the cheek

a rule are carried out under general anesthesia In cases in which a flap from the trunk is utilized the primary stage in which the flap is tubed is performed with general anesthesia Intratracheal anesthesia with the tube inserted through the nostril also is extremely satisfactory for this purpose particularly at the time the flap is transferred since it permits a clean field to be maintained, the anesthetist is well back out of the way and the anesthetic is well controlled In addition, the pharynx can be tightly packed off to eliminate the hazard of blood entering the air passages

The improvement in the general health of the patient which follows repair of long standing operative defects of the lips and cheeks often is marked and manifested promptly While in many instances there is little evidence that the perforation into the mouth produces a detrimental effect on the general health of the patient, some of these individuals become markedly dehydrated and anemic, and have difficulty with elimination This apparently is the result of loss of fluid in the saliva, which drools through the operative opening and the lessened fluid and caloric intake which are occasioned by increased difficulty in eating and drinking After correction of these conditions, following closure of the opening, the general health of the patient often improves decidedly and there is considerable gain in weight An equally important feature in this regard is the notable change in the mental attitude which is incident to the discarding of the dressing that has been worn on the face for a number of months

No originality is claimed for any of the operative procedures employed Many are very old and some bear the names of their advocates

CONDITIONS NECESSITATING SURGERY FOLLOWING CHOLECYSTECTOMY[1]

An Analysis of Sixty-six Cases and a Discussion of Certain Technical Problems Concerned in Removal of the Gall Bladder and in Operations upon the Common Bile Duct

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FOLLOWING removal of the gall bladder, conditions demanding further surgical therapy may develop during the period of post-operative recovery, or later as a complication of or sequel to, the biliary tract disease or because of mishaps incident to the procedure itself.

This survey is an analysis of 66 cases re-operated upon in the University Hospital over a period of 15 years, following cholecystectomy. Inasmuch as patients sent to this hospital are committed from all of the counties of the state of Iowa, it would seem that this survey fairly represents the experience of the medical profession of the commonwealth, together with that of the Surgical Service of the University Hospital.

All patients who have had cholecystectomy performed in this hospital or elsewhere are included in this series if they have required subsequent surgical attack. In some of the patients attack was made, at the time of original operation, upon the common duct in addition to cholecystectomy. In a large majority the appendix was removed. An analysis of the 66 cases comprising this survey shows that they fall rather definitely into 6 well defined groups. In addition to these groups, there are a few cases of miscellaneous character.

1. *'Reformed gall bladder' - 14 cases.* The term 'reformed gall bladder' is used, as it seems to express a clinical situation in respect to symptomatology even if it is a misnomer pathologically. On the basis of the findings it seems reasonable to explain the development of a pouch simulating a gall bladder as due to the dilatation of a cystic duct stump. The pouch commonly varied from 1 to 2.5 inches in length and was usually of the caliber of one's little finger. It was often clubbed in shape. In the occasional case, the pouch was of such size and configuration as to suggest that division had been made across the gall bladder wall at the time of cholecystectomy.

The pathology was characterized in every instance by extensive adhesions which hid the hilus of the liver, the common duct, and the "new" gall bladder. Upon exposure of the major ducts by dissection, the "reformed gall bladder" was found "frozen" to the hepatic duct in 4 cases, and to the common duct in 2. In such instances a ready explanation for the patient's symptoms was at hand. In 5 there was angulation of varying degree of the major ducts and usually at the junction of the common hepatic with the common. In some, this distortion was so marked that obstruction in considerable degree was produced. In 4 patients the gall bladder contained calculi.

Associated pathological change was not as commonly found as might be expected. In only three instances was there present a stone in the common duct, and in one of these there was marked cholangectasis. In another there was a marked inflammation of the common duct beyond that of the neighborhood inflammation from the adherent 'new' gall bladder. In 1 patient a fistula was present between the gall bladder and duodenum and in this tract were present small calculi. In several there were varying shades of chronic pancreatic inflammation, and in one in whom this was quite marked following re-operation, death occurred from acute exacerbation. Hepatitis of some degree was present in a few cases in addition to cholangectasis as noted in the patient just referred to. In no other instance was it very marked.

The interval elapsing between cholecystectomy and the onset of symptoms varied considerably. In 2 cases there seemed to be no clear interval before symptoms recurred after operation. In 5 cases the interval was somewhat short of a year, while in 4 it was over 5 years. Following the development of symptoms, 2 of these patients required re-operation within less than a year while 9 of them did not seek further surgical attack until after 5 years had elapsed.

In the majority of cases the symptoms were described as being identical or similar to those of the original trouble. In 3 patients who had had questionable or definite jaundice with the original trouble, this symptom was present in the recurring attacks. In 6 others jaundice of some degree developed with the new difficulty when it had not been present with the original trouble and in 3 of these jaundice was marked.

An analysis of the pathological findings in this group together with the symptoms from which the patients complained leads to the conclusion

[1]From the Department of Surgery, College of Medicine, University of Iowa. Presented before the Western Surgical Association, St. Louis, December 7, 1934.

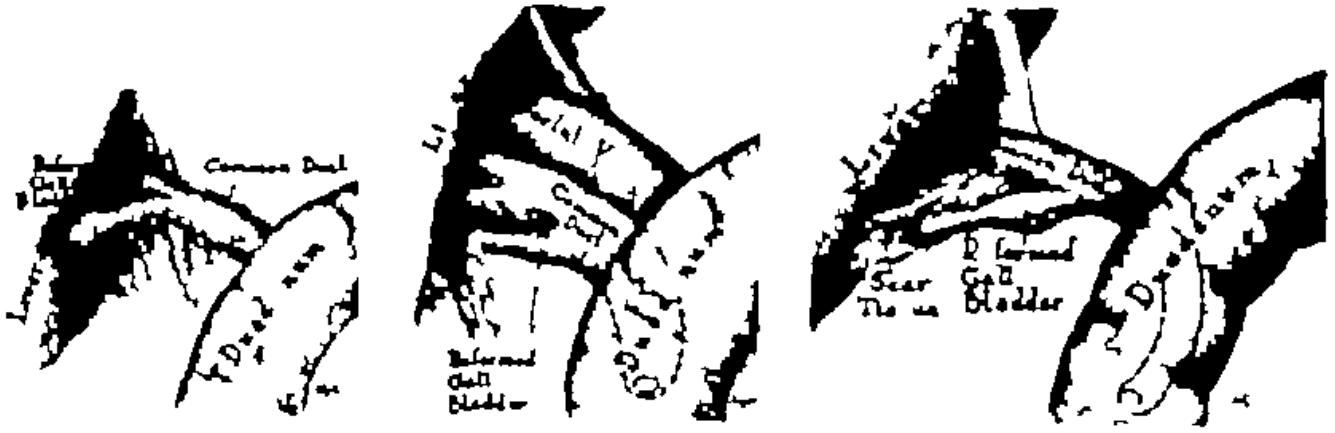


Fig 1 Three cases of simple reformed gall bladder one of which contained a calculus

that a "reformed gall bladder" is a definite entity as a sequel to cholecystectomy and that it may be responsible for symptoms and complications similar to those developing in a diseased gall bladder In any given case however in which there was present associated pathological change it was impossible to ascribe the patient's complaints entirely to the "new" gall bladder The latter might be an accidental finding

Certainly in the 3 patients in whom the common duct harbored calculi, the symptoms cannot be charged solely against the new gall bladder The stones may have been present at the original operation. In one case however the stone found lodged in the common duct ampulla was of the size and shape of the "new gall bladder suggesting that it may have represented a cast of the pouch and had been extruded into the common duct.

It seems reasonable to conclude that not only may a "reformed gall bladder" be responsible for symptoms but that it should be chargeable to ineffectual surgery In this clinic, emphasis has been placed upon the advisability of ligating the cystic duct close to its junction with the common when cholecystectomy is performed therefore it is of interest to note that of the 14 cases in this group only 1 had been operated upon originally in this hospital.

B. Injury to the major ducts—11 cases Surgical trauma to one or other of the major bile ducts as a complication of cholecystectomy is one of the serious hazards in this operation In this series the postoperative course presented a fairly definite and rather common clinical picture. In some in whom drainage had been provided for through the abdominal wall, bile began to flow copiously almost immediately following operation and persisted as a biliary fistula until re-operation was carried out at a varying time subsequently In others a period of 24 to 72 hours elapsed, during which time the patient became markedly jaundiced. Biliary drainage then established itself and there was improvement in the symptoms In others the bile drainage having been maintained for many weeks finally stopped and the patient then became jaundiced and often had associated chills and fever In 2 of the 11 cases, an anastomosis had been made between injured duct and duodenum before the patients came to this clinic and presented themselves here because of recurring difficulty In one it was because of stricture of the anastomosis and in the other the symptoms were best explained on the basis of a pancreatitis.

The pathology involving the traumatized ducts was as follows In 2 there was present an incomplete stricture at the junction between common and hepatic ducts which seemed to suggest that ligation of the cystic duct had included a considerable portion of the adjacent wall of the major duct and in 1 of these there was angulation in addition to the narrowing and scar The common duct had been completely severed in 9 cases in 4 the patient entered the hospital with a biliary fistula which led to the dilated stump of the hepatic duct while in the 5 remaining cases the incision had healed and the patient was deeply jaundiced at the time of re-operation Two of these were the patients described who had been re-operated upon prior to entrance to this hospital In 1 of these 5 the divided hepatic duct was represented by a mass of scar of such extent that no lumen could be found, although the dissection was carried to a high level into the hilus of the liver Obviously the situation was not remediable and the patient succumbed

In 1 of the 11 cases cholecystectomy had been performed in this clinic Recognition of the fact that a portion of the common hepatic and com-

mon duct had been removed with the cystic duct, was made after the operation was completed and the specimen studied By that time it did not seem that the patient's condition warranted immediate re operation and reconstruction of the severed ducts Biliary drainage established itself 3 days later and the jaundice which had developed cleared up promptly The bile continued to drain through the incision freely but the patient succumbed from sepsis on the twentieth day after operation Immediate re-operation might have been the wiser choice In 2 other cases in this clinic the major ducts have been divided in the performance of cholecystectomy and with recognition of the situation during operation Immediate reconstruction was made in each with a successful result in 1 and a fatality in the other

The operative procedures which have been carried out in the 11 cases have varied with the condition encountered In 5 it consisted of anastomosis between hepatic duct stump and duodenum, with a satisfactory biliary drainage into the bowel in 4 of these In the fifth case, the patient in whom an anastomosis had been made elsewhere, the patient developed a massive stricture of the hepatic duct at the site of anastomosis and was operated upon in this clinic on three occasions in an attempt to maintain a permanent lumen Following each operation, there was a period of 6 to 14 months of freedom from symptoms to be followed by recurrence of chills and jaundice as the stricture reformed The patient finally succumbed

In 2 patients anastomosis was made between the hepatic and common duct stumps over a "T" tube In 1 the result was satisfactory In the other a stricture developed after a period of several months, and at re-operation reconstruction of the duct at the site of stricture was made over an internally placed tube This has been followed by a 6 year cure

In 2 patients drainage of the dilated hepatic duct stump was carried out as a palliative procedure to get the patient in better condition for a reconstruction operation One patient died The other was found to have multiple chronic abscesses of both lobes of the liver Her condition improved very markedly but she refused further surgical treatment and returned to her home with a draining biliary fistula

With an analysis of the experience in this clinic with cholecystectomy and of these cases as a basis, it would seem that injury to the major ducts is more likely to occur in cases in which the technical difficulties of cholecystectomy are relatively slight In pulling upon the gall bladder

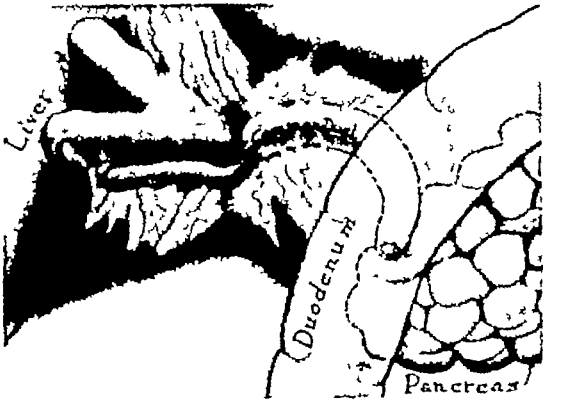


Fig 2 "Reformed gall bladder" associated with angulation and constriction of the common duct together with considerable thickening of the pancreas The "new" gall bladder was tightly adherent to the common hepatic duct.

as a means of exposing its cystic duct, a sharp angle may easily be produced at the junction of common hepatic and common ducts so as to bring the common duct and the cystic duct in the same line and make the common duct seem a continuation of the other It is easily explainable why, in such an instance, a clamp or ligature is thrown around the common duct and a segment of it taken away This is likely to occur when the ducts and the gall bladder are relatively elastic and the procedure seems to be simple In cases in which the disease of the gall bladder and the pericholecystic structures is more marked, the surgeon is likely to proceed with greater care and tugging upon the gall bladder is less likely to angulate the major ducts

C Common duct stone—6 cases In 6 patients re-operated upon following cholecystectomy, the major pathological finding which reasonably explained the recurrence of symptoms consisted of calculi in the common duct In 3 other instances, as stated in the discussion of "reformed gall bladder," stones were present in the duct

In these 6 patients an analysis of the symptoms antedating cholecystectomy and those which followed the operation lead to the conclusion that the calculi were present in the common duct at the time cholecystectomy was performed without much question in 2 instances and probably in a third In a fourth case the findings at operation were such as to make it unlikely that stone was present in the common duct when the gall bladder was removed In the 2 remaining cases in addition to cholecystectomy the common duct was opened for the removal of stones and in each instance the duct was of such caliber that the

Fig 3, left Reformed gall bladder" associated with angulation of the common duct and calculus in the ampulla of Vater The stone was of the size and configuration of the "new" gall bladder and suggested that it probably had formed within it, to be subsequently extruded

Fig 4 Reformed gall bladder" with a fistulous tract communicating with the duodenum The common duct was angulated and somewhat constricted

little finger could be introduced within it and an accurate determination made that no stones were left behind. In each the patient returned after a period of many months with recurring trouble and at re-operation new stones were removed from the duct In each again the finger could be used to prove that all calculi had been taken away In one of these patients, after an elapse of several more months, stones of considerable size reformed once more

The incidence of common duct stone in these 66 cases of re-operation following cholecystectomy would seem to be surprisingly small comprising as it does only 6 The development of calculi in the common duct was proved to have occurred in at least 2 cases *following* cholecystectomy and it probably took place in 2 others.

D Angulation of the common duct—3 cases In addition to those patients who suffered trauma to the major ducts at the time of cholecystectomy or who harbored stones in the common duct either before or after cholecystectomy there were 3 patients who required operative treatment because of mechanical distortion These are in addition to those patients who had pathological changes of this character in association with a reformed gall bladder as already described

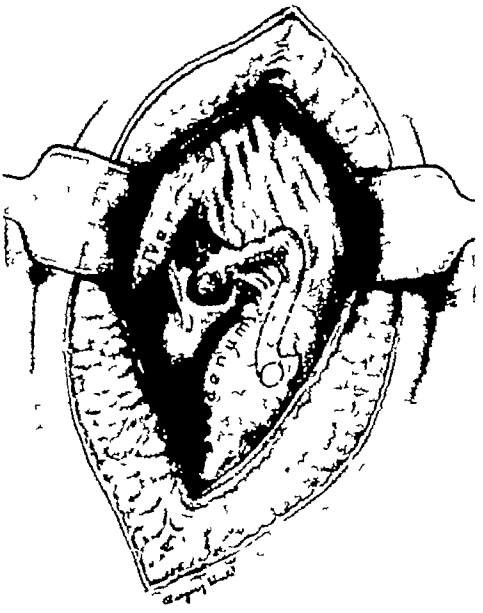
In 1 instance there was found a stump of cystic duct about three fourths of an inch long but which was not dilated and could not properly be classified as a 'new gall bladder This cystic duct stump was fixed to the gall-bladder bed by scar and sharply angulated the major ducts in consequence A second patient, operated upon in this hospital, had a cholecystectomy and drainage of the common duct following the removal of many common duct stones Two weeks following the removal of a "T" tube, which had been placed in the common duct for drainage, the patient developed an attack of pain associated with jaundice At re-operation 7 months later with a pre-operative diagnosis of common duct stone, no calculi were found but there was present a very sharp angle between common hepatic and common ducts at the site of the former tube drainage This distortion was produced by scar to the gall bladder bed in the liver

RECAPITULATION

A review of the cases in the four groups just described suggests certain points in respect to the technique of cholecystectomy and common duct surgery

It is quite clear that a surgeon must chart an accurate course across the cystic duct to avoid the Scylla of a "reformed gall bladder" on one side and the Charybdis of major duct injury on the other The answer does not seem to lie in one s choice of performing cholecystectomy by beginning the dissection of the gall bladder at the fundic end or only after the cystic duct has first been exposed and divided On the basis of personal experience with each, it would seem that both modes carry the same inherent dangers In this clinic, as a routine, removal of the gall bladder is begun at the cystic duct end

Accurate identification of the cystic duct in relation to the major ducts is essential to division



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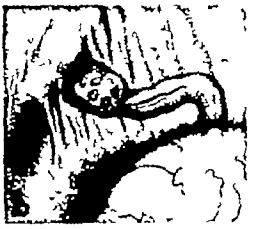

Fig 5 a, "Reformed gall bladder" containing a calculus, with marked angulation and constriction of the common duct. The dilated hepatic ducts contained many calculi b The constricted common duct after the "new gall bladder" was dissected free and removed The biliary tree was subsequently visualized by the introduction of lipiodol through the draining "T" tube for roentgenographic study, and marked cholangectasis was shown

of it at the proper level This is difficult in cases in which there is present a massive inflammatory reaction, recent or old, in the mesocysticum, and especially if there is distortion of the anatomical relationships from scar contraction A careful deliberate dissection is necessary, and it is best carried out bluntly There is no need for isolating the cystic artery independently After the cystic duct has been completely freed in a given area from the cellular tissue in the mesocysticum, any traction applied through the gall bladder should be relaxed so as to permit the major ducts and the cystic to assume their normal positions, and only then should a clamp be placed across the latter This should traverse the cystic duct at its junction with the common and the jaws of the clamp must not include any of the tissue beyond the isolated duct A second clamp is then applied parallel to the first and division made between them

A curved hemostat is now placed close to the proximal stump of the duct and the gall bladder, and directed obliquely across the mesocysticum toward the gall-bladder bed This will usually include the cystic artery if the latter has not already been secured by the clamp across the cystic duct With scissors, division is made between the hemostat and gall bladder

Before proceeding with further dissection of the gall bladder, the clamp on the mesocysticum is replaced by ligature following which the duct stump is ligated Two ligatures of No 3 plain catgut are placed on the stump This heavy ligature is used as it does not cut the duct and lead to biliary leakage

In proceeding with the removal of the gall bladder, incision is made through the peritoneal investment on each side so as to leave flaps, and these are sutured across the gall-bladder bed to control oozing and to minimize the raw surface to which adhesions may form with adjacent viscera This is important as a means of preventing angulation of the major ducts and angulation and fixation of the pylorus or duodenum from scar

In cases in which attack is to be made upon the common duct in addition to cholecystectomy it is usually best to proceed with the former as the first step because the gall bladder and its duct may be invaluable for a landmark and for traction

In respect to the problem of common duct stone, a surgeon is faced with the humiliation of failing to detect and remove a stone on the one hand and certain postoperative complications and sequelæ from opening a common duct

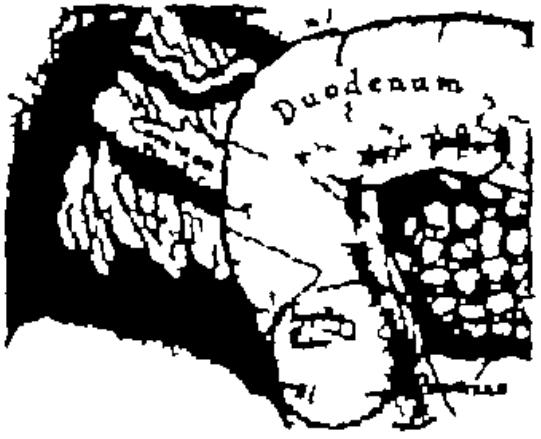

Fig. 6 Large calculus in the ampulla of Vater which probably developed following cholecystectomy. Note the unusual position of the papilla of Vater (incorrectly labeled ampulla) due to the marked pouching of the duct.

needlessly on the other. *The common duct cannot be opened with impunity.*

In every patient upon whom operation is performed for gall-bladder disease in an interval between attacks examination by palpation of the common duct should be carried out routinely. As has been emphasized by Bevan this is best done by standing upon the patient's left side and passing one's left index finger behind the gall bladder so that it enters the foramen of Winslow and is, therefore directly behind the common duct. With the thumb in front palpation can be carried out along the entire extent of the duct and the pancreatic head. It is in the latter region that a stone is most likely to be missed.

While many writers have stressed the fact that common duct stones may be symptomless, special attention to possible stone in the common duct is given to patients in whom jaundice in any degree has been present in any attack or in whom apparently uncomplicated gall bladder attacks have been associated with chills. A dilated common duct should arouse interest in a possible common duct stone, although a shriveled completely functionless gall bladder commonly leads to functional dilation of the common duct of considerable degree.

When drainage of the common duct by "T" tube is instituted, great care is taken to repair the duct incision accurately to the point of emergence of the vertical limb. For this No. C machine twisted silk on a fine curved needle is used with interrupted stitches and each bite picks up the full thickness of the duct wall to include the mucosa. This has proved more efficient than catgut either as a running or interrupted stitch. After cholecystectomy is completed, a running stitch of fine catgut repairs the serosa over the common duct to cover the suture line in the latter, and is continued on to the gall bladder bed.

The "T" tube is brought through the incision or through a stab wound to the right, depending upon which point seems more direct. The tube in its position between common duct and parietal peritoneum *must not be too taut* or angulation of the major ducts may be produced and this lead to permanent distortion or predispose to narrowing or scar constriction subsequent to removal of the tube. With marked distention of the abdomen or in violent movements of the abdominal wall during vomiting or coughing, after operation, the tube may become dislodged from the sutured duct, the suture line give way or the duct may be completely torn across.

Injury to the common and hepatic ducts during cholecystectomy or from inflammation, or due to postoperative mishaps, leads to pathological situations of grave surgical import. Each case is a distinctly individual problem. Not the least of the technical difficulty is due to the extensive adhesions which are invariably present and the necessity for a painstakingly careful dissection to expose the biliary tract and avoid injury to adherent viscera.

If the major duct has been completely severed and a fistulous tract leads from the skin to the hepatic stump exposure of the latter is relatively easy. With or without a fistula, the stump is usually dilated and tense and may contain calculi. The duodenal end may be short and so small in caliber and buried in scar that it cannot be recognized without a retrograde sounding through the opened duodenum—a procedure of questionable merit.

End-to-side anastomosis between the stump of the duct and the adjacent duodenum is usually the operation of necessity. Mobilization of stump and bowel should be done to permit of union without tension. Interrupted stitches of twisted silk are used, accurately placed so as to pick up the full thickness of duct and duodenal wall. In uniting the posterior margins, the stitches are placed within the lumina and the knots be in contact with the mucosal junction. When the angle is reached above and below and suture of the anterior margins is made, the stitches are placed so that the knots be externally. *Accurate contact which includes mucosa is essential* to obtain substantial union and to minimize the danger of subsequent stricture. Reliance upon a rubber tube to bridge a gap between duct end and duodenal wall is hazardous. The scar tissue which reforms the duct in the gap is very likely to contract after the tube has passed or has been

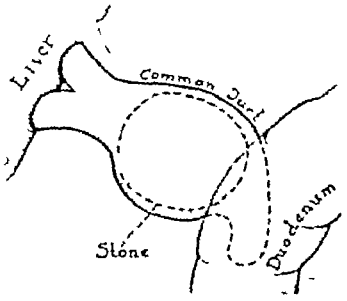

Fig 7

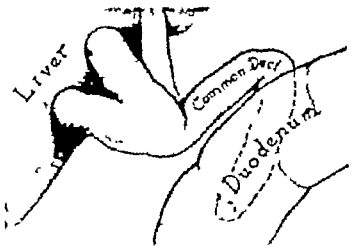

Fig 8

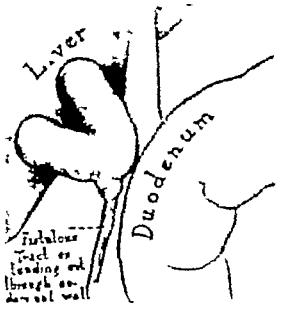

Fig 9

Fig 7 Bantam egg sized calculus in the midportion of the common duct which presumably developed following cholecystectomy The patient was free of symptoms for 5 years following removal of the gall bladder

Fig 8 Marked angulation producing obstruction of the common duct following the operation of cholecystectomy

Fig 9 Injury to common duct which was incurred during cholecystectomy followed by the development of a biliary fistula leading to the greatly dilated stump of the hepatic duct

removed (where a "T" tube is used) and a hard, impermeable stricture develops

The suggestion has been made of utilizing a fistulous tract from skin surface to duct end as a means of establishing a communication with duodenum or stomach, by mobilizing the fistula by dissection, and introducing the skin end into bowel or stomach As the fistulous tract is usually tortuous and narrow and lined throughout with scar, or unhealthy granulation tissue, this procedure seems of very dubious value

In some cases of complete division of the major duct, the duodenal segment lies in close proximity to the hepatic stump so that end-to-end reunion of the two is possible The duodenal portion of the duct is often of small caliber and the disproportion between it and the dilated hepatic segment is marked Dilatation of the small calibered portion is often feasible until approximately the same size as the other In this clinic, special sounds[1] have been devised for this purpose, of such length, curvature, and gradation as will permit of their ready introduction into the duct and its gradual dilatation without injury

Obstruction of the duct by intrinsic scar is usually a difficult condition to remedy Sometimes the stricture is limited to a small segment of the duct, as it may be when it develops at the site of former "T" tube drainage, or following incomplete division during cholecystectomy Depending upon the degree of obstruction, the proximal segment is dilated and often contains stones or "bile mud," and the distal segment is usually contracted

In such a case the operative attack may be relatively easy and will consist of an incision in the long axis of the duct to straddle the stricture The proximal limb is emptied of any foreign material by forceps and saline flushing, and the distal limb is carefully and gradually dilated by sounds until it is approximately the caliber of the proximal The incision is then closed by interrupted sutures, *in the transverse axis of the duct* This secures a liberal lumen at site of stricture This procedure is not feasible if the duct wall on either side of the stricture is thickened and inelastic

When the duct is extensively involved by scar there are three courses for the surgeon to pursue Which one shall be chosen in a given case is an individual problem and may be difficult to decide Before he is through with the case, the surgeon is likely to wish that he had decided differently These consist of (a) resection of the scarred segment of duct and re-establishment of continuity by end-to-end anastomosis, (b) division of the duct proximal to the scarred area to be followed by anastomosis between the duct end and the side of the duodenum, (c) dilatation of the contracted duct, and drainage of it by tube for a long period of time

The latter course usually will be the only feasible one, due to the extent of the pathological change in the duct The terminal portion is often markedly involved and the duodenal wall at the site of emergence of the duct is commonly indurated and unyielding and producing obstruction It is in a situation of this sort that the graded common duct sounds have proved invaluable in this clinic. The duct is incised in its long axis and in the most accessible area The largest sound which can be introduced without force is selected, anointed with liquid petrolatum, and slowly and gently passed to the left until it enters the duodenum through the papilla of Vater

[1]These are of value in any case of surgery of the common duct to outline the course of the duct or to determine the presence of calculus Before introducing a sound, it is anointed with liquid petrolatum

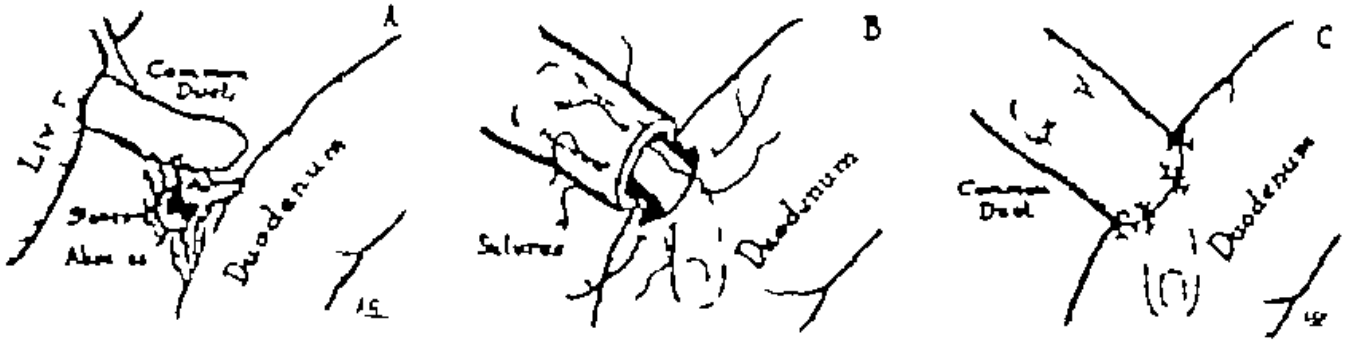

Fig. 15. A, Injury to common duct during cholecystectomy with closed dilated duct stump. A small chronic abscess containing calculi is present and has established drainage through the wall of the duodenum. B, Anastomosis between the duct end and the side of the duodenum was made, enlarging the opening in the latter through which the abscess is draining. C, Completed anastomosis. Suture is made over a piece of catheter and a rubber flange constructed to help maintain the tube in position for considerable time.

It is then withdrawn and passed to the right. The next largest sound is now used, by gradually increasing the size of the sounds, and always working with great gentleness and deliberation, a surprising degree of dilatation can be obtained in the majority of cases, and without trauma to the duct.

Drainage of the duct should be established by either the internal or external route. For the former a catheter may be used of such size as will easily lie within the dilated duct and papilla of Vater. Its duodenal end should protrude 2 to 4 inches into the bowel, and the proximal end extend well to the right of the incision in the duct. The latter is accurately closed by interrupted stitches of silk and reinforced by a serosal stitch of catgut. The method of internal drainage is ideal in these cases except that one has no accurate control over the length of time during which the tube will be maintained in the duct. Without some mode of fixation the tube will usually be passed into the bowel in from 7 to 14 days, which is unfortunate because recurrence of the common duct scar contraction usually follows. Some control of the tube in the duct can be secured as shown in Figure 13. By this technique the tube will remain in the duct from about 3 weeks to years, depending upon the maintenance of the suture material in the duct wall.

Drainage by the ordinary "T" tube offers a means of control of the period of drainage. The outstanding objection to its use lies in the fact that the intraductal portion of the tube is not sufficiently long to pass through the papilla of Vater and this segment of the duct may promptly close down following dilatation.

In this clinic a special "T" tube is used in cases of this sort with a long intraductal portion. The duodenal end is cut off at a point which permits it to be within the bowel for a distance of 2 to 4 inches beyond the papilla of Vater. As in all cases of "T" tube drainage, suture of the duct wall around the external limb is carried out with the utmost care.

Following operation, fluid can be safely given through the tube if desired, and in all cases, after the first few days after operation, from 200 to 300 cubic centimeters of warm tap water are introduced into it daily to keep it flushed out. This causes the patient no concern. In fact, there is no sensation whatever produced in most instances. The tube can be maintained in place for an indefinite period of time and is just as easy of removal as is the ordinary type. One patient has worn such a tube for nearly a year without difficulty, and her common duct was so markedly pathological, that the tube will probably be left *in situ* as long as she lives. Twice each day she introduces a small amount of water into it through the external limb and the rest of the time shuts it off by a rubber band.

E. Faulty repair of the incision—19 cases. Following cholecystectomy difficulty in respect to the incision may develop as an early postoperative complication or at a varying period of time later after healing has been apparently complete.

Wound separation occurred in 8 instances and of course represented cases operated upon in this hospital. Only such cases are included in this group as were treated by resuture rather than by any form of non-operative support. The degree of separation varied but in most instances would be classified as complete and associated with some evidence of evisceration. This alarming complication sometimes developed abruptly but in most cases there were symptoms which suggested that separation of the wound had begun in the deeper layers before the evidence of the serious situation was manifested through the skin incision. In 4 patients there was rather

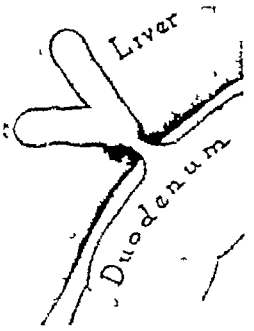

Fig 11 Development of excessive scar with resulting stricture and obstruction at the site of anastomosis between hepatic duct stump and duodenum The common duct had been injured during cholecystectomy

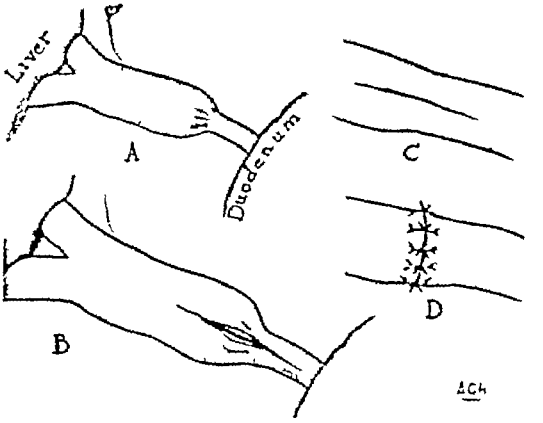

Fig 12 A method of attacking a stricture of the common duct limited to a short segment of the duct Following incision through the stricture in the long axis of the duct, *B*, the contracted distal segment is dilated by graded common duct sounds until it is approximately the caliber of the proximal portion, *C*, and then the incision in the duct is sutured in the transverse axis *D*

obstinate vomiting in the early postoperative course suggesting a potent etiological factor In 1 case there was obvious wound infection In only 1 of the 8 cases was cholecystectomy associated with common duct drainage The separation occurred through the sixth to the twelfth postoperative day, the average being the ninth day

The seriousness of this complication is shown by the death of 4 of these 8 patients

Incisional hernia requiring surgical repair occurred in 11 patients, of whom 5 had had the cholecystectomy performed in this hospital In this group of 11 the presence of a hernia was manifested in 2 as soon as the patient got up following operation In 1 patient the interval was 5 years In 8 of the 11 patients herniation was noted at some time during the first year As a predisposing factor in the postoperative course, vomiting was pronounced in 2, a cough was blamed in 2, marked distention in 1, and a wound infection in 1 In the rest of the cases no predisposing factor could be elicited either from the history or the record

Undoubtedly, incisional hernia following cholecystectomy occurs much more frequently than this small group of cases signifies A hernia in the right upper quadrant may be complacently tolerated by a patient and often an abdominal support will control distressing symptoms Danger of strangulation is relatively much less than in incisional hernias in the lower half of the abdomen

Postoperative wound separation or the subsequent development of an incisional hernia cannot lightly be ignored as a complication of, or sequel to, cholecystectomy In the former the risk to life is great, and in the latter the disability may be marked The importance of adequate and secure closure of the abdominal incision at the time of cholecystectomy cannot be sufficiently stressed to a surgical staff Closure of the incision is boresome to many surgeons and is commonly delegated to some junior, in spite of the fact that this portion of the operation will occasionally be as difficult and require as much skill and attention to detail as the removal of the gall bladder

The conclusion has been arrived at, from an analysis of cases of wound separation in this hospital and operations for incisional hernia following cholecystectomy, that the posterior sheath of the rectus commonly gives way first which leads to a wide separation of the peritoneum and, what is more important, of the transversalis This puts an undue stress upon the anterior sheath which either soon gives way because of the tearing through of sutures, or at a later time begins to stretch until a hernia is the end-result

A deep wound separation often produces a clinical picture which is diagnostic It is that of a high incomplete intestinal obstruction and the outstanding early symptom is repeated vomiting One is likely to blame the vomiting for the giving way of a wound, whereas it is really an effect rather than a cause When the abdominal wall gives way from within, the pyloric end of the stomach and first portion of the duodenum or loops of jejunum or ileum, together with omentum and hepatic flexure of the colon, may fill the deeply situated defect Distortion of the gastrointestinal tract may take place to produce me-

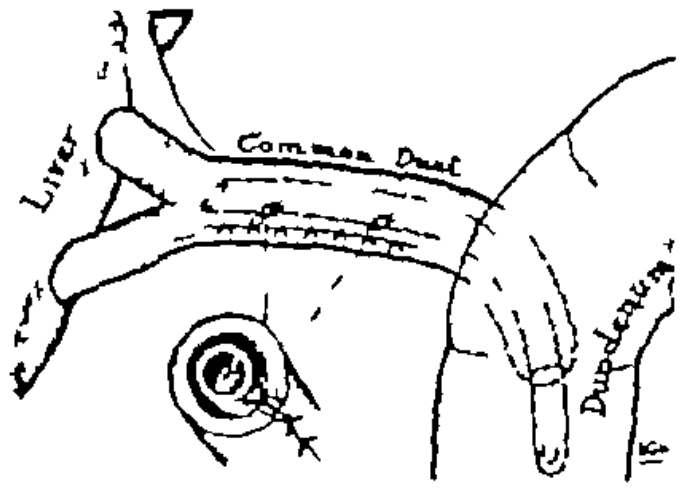

Fig 3 T demonstrate a simple way of maintaining an internally placed tube within the common duct for considerable time Loops of silk are placed in the side of the tube and these are caught in interrupted stitches which close the incision in the duct The tube will pass into the intestinal tract when the stitches finally work through the healed duct wall

chanical obstruction in considerable degree and abdominal distention follows. There may be no undue elevation of temperature or leucocytes, the wound appears to be secure, and the patient is usually treated for paralytic ileus

In this hospital there has been a very definite decrease in the incidence of postoperative wound separation and in the development of incisional hernia with the passing years. It is felt that this is due to two factors (1) Constant emphasis has been placed upon the importance of meticulous care in incisional closure. The necessity for including the transversalis muscle as well as the peritoneum in the suture of the posterior rectus sheath is stressed. It has been found that a generous bite of the posterior sheath parallel to the incision, rather than at right angles to it, tends to minimize the tendency of this structure to split A running stitch of doubled catgut is used and this is locked frequently as it is continued A proper closure is often time-consuming but it is time well spent (2) The use of ethylene for basal anesthesia. While ether must usually be added, it is in relatively small amounts and the incidence of postoperative vomiting and pulmonary complications with cough is definitely lessened

F Postoperative infection within the peritoneum —6 cases These patients were all operated upon *in this hospital* and with one exception represented conditions with marked pathology In 4 of the latter besides cholecystectomy, the common duct was opened for the removal of stones.

In 1 patient a pelvic abscess developed as a postoperative complication which was drained through the rectal wall with recovery In 2 patients a subhepatic abscess formed. In 1 this developed during convalescence and the abscess contained bile as well as pus. In the other many weeks elapsed but the same character of content was present in the abscess and the latter led to the stump of the cystic duct In each case the establishment of adequate drainage was followed by a prompt recovery

In the 3 remaining patients the infection developed under the diaphragm and in each it was situated posteriorly In these cases no bile was present within the abscess. In 2 of this group pericholecystic abscesses were present at the original operation in addition to stones in the common duct. In all of these cases the subphrenic abscess was drained through the thoracic wall posteriorly with recovery

In another case not included in this series, there was clinical evidence of a subphrenic accumulation of considerable amount. The first stage of a planned 2 stage drainage through the thoracic wall posteriorly was performed. A few days later very free drainage of bile was spontaneously established through the abdominal incision with complete relief of all symptoms, and the patient went on to a cure without completion of the subphrenic drainage.

The possibility of contamination of the general peritoneal cavity by septic material is obvious in any operative attack upon the biliary tract. This danger is increased when the procedure is technically difficult and when infected bile escapes in quantity from opened duct or gall bladder To prevent widespread contamination, great care should be taken to protect the operative field by properly placed lap pads, and the generous use of a "sucker throughout the operation is a potent means of controlling the dissemination of infected fluid into the peritoneal cavity

The deep recess below and behind the gall bladder is an especially critical area because infected material can so easily gravitate into it and subsequently infection may spread between liver and diaphragm to produce a subphrenic abscess It is wise to carry a strip of iodoform or plain gauze into this area as a coffer dam before proceeding to any attack upon common duct or gall bladder At the conclusion of the operation a strip of gutta percha or small tube had best be carried to this area for drainage

G Miscellaneous—8 cases Cholecystectomy was performed in this clinic on a patient in whom there was a recurrence of similar attacks after a lapse of 3 months Before and following operation there had been chills and some degree of jaundice

Fig 14 Diverticulum of the duodenum at the site of the papilla of Vater This produced symptoms suggesting cholecystitis and led to cholecystectomy The symptoms recurred, and restudy of the patient disclosed the diverticulum He has been cured by anastomosis between the enormously distended common duct and the duodenum The diverticulum was situated in the posterolateral aspect of the second portion of the duodenum The latter and the common duct are shown in a rotated position to demonstrate the diverticulum

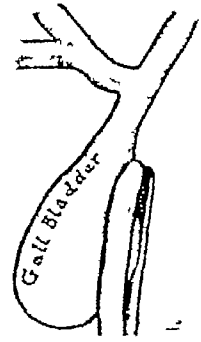

Fig 15 To show how traction upon the gall bladder during cholecystectomy will bring the cystic and common ducts into the same line The surgeon may then mistake the common duct for the cystic and crush it by clamp or ligature

with the attacks No stones had been found in the common duct and the pancreas seemed normal At re-operation there was no evidence of a "reformed gall bladder' the pancreas and liver both seemed normal The common duct was opened and no stones were present within it It was dilated so that the little finger could be used for palpation The wall was considerably thickened and subacutely inflamed This seemed to represent a condition of common duct inflammation independent of other demonstrable causes

A patient developed attacks of biliary difficulty 3 years following cholecystectomy and operation was begun but terminated because of injury to the duodenum Patient succumbed and postmortem examination uncovered an acute pancreatitis together with marked chronic change in this organ The common bile duct presented no evidence of pathology and contained no stones and the liver was normal

Cholecystectomy was performed for symptoms strongly suggesting biliary tract disease associated with jaundice The patient had syphilis Adequate explanation for her difficulty seemed to lie in gall-bladder disease There was no evidence of disease of the liver Symptoms recurred after a period of 1½ years Re-operation uncovered no satisfactory explanation for the recurrence of symptoms on the basis of demonstrable disease in the biliary system including the pancreas

Cholecystectomy was performed here with a diagnosis of recurring cholecystitis No stones were present, but the gall bladder seemed to present satisfactory evidence of disease to explain the symptoms Two years later the symptoms recurred but were associated with chills There was no jaundice Pre-operative study disclosed the presence of a diverticulum of the duodenum in its second portion At re-operation a common duct 5 centimeters in diameter was disclosed and a diverticulum the size of a hazelnut was present in the region of the papilla of Vater The common duct was opened and found to contain no stones An anastomosis was made between it and the duodenum The patient has been relieved of all further symptoms for 2½ years

Cholecystectomy was performed in this hospital and on the second day continued bleeding manifested itself through the wound Incision was reopened and large clots together with fluid blood were found in the operative area There was no active bleeding point.

Cholecystectomy in this hospital was followed on the tenth postoperative day by the symptoms of intestinal obstruction Operation was performed and a loop of small intestine was found tightly adherent at the lower angle of the wound Possibly it had been fixed in the peritoneal suture The patient succumbed

Cholecystectomy performed here was followed by obstinate vomiting which persisted for 5 months Re-operation disclosed a pyloric obstruction due to fixation of the pylorus and first portion of the duodenum against the liver in the hilus area. Posterior gastro-enterostomy was performed with an excellent result In a somewhat similar case a second operation was done elsewhere and

therefore is not included here. In this instance the obstruction manifested itself during the hospital convalescence. Re-operation was carried out on the twelfth postoperative day Gastro-enterostomy was followed by complete recovery Adhesions between the viscera in the hilus area and especially involving the duodenum always develop in some degree after cholecystectomy and are probably responsible for some of the lesser complaints following operation Careful handling of tissue complete hemostasis and peritonealization of the gall-bladder bed by suture will tend to minimize the formation of adhesions

Cholecystectomy was performed on a patient in this hospital and a stone impacted in the ampulla of Vater was removed A small opening was inadvertently made in the posterior wall of the duodenum by a probe passed into the common duct. This opening was repaired by suture During postoperative recovery a duodenal fistula developed which failed to respond and gradually increased in size and in the amount of leakage. After many days the patient was re-operated upon. A posterior gastro-enterostomy was performed and the pylorus excluded by ligature in the hope of diverting the gastric content away from the duodenal leak. The patient succumbed

CONCLUSIONS

1 A "reformed gall-bladder may develop from dilatation of the stump of the cystic duct following cholecystectomy This may undergo pathological changes and be responsible for pathological complications and produce symptoms in the same manner as a diseased anatomical gall bladder It is chargeable to ineffectual surgery and can be prevented by ligating the cystic duct close to its junction with the common

2. Injury to the major ducts is a constant hazard in the performance of cholecystectomy and leads to a critical situation which will require further surgical attack The injury will vary from inclusion by ligature of a small portion of the side of the duct wall, to excision of a large segment of it.

3. In the performance of cholecystectomy accurate identification and exposure of the cystic duct is essential Avoid distortion, by traction upon the gall-bladder wall, of the anatomical relationships between the major ducts and the cystic when applying a clamp or ligature across the latter

4 Stones in the common duct may be overlooked. Careful examination of the duct for possible stone should be made in every case before removal of the gall bladder even though there have been no symptoms suggesting common duct stones. Of special significance are the history of jaundice in any degree during any attack, or the history of chills during attacks, which otherwise suggest uncomplicated gall-stone colic or the finding of a dilated common duct at operation Opening of the common duct for exploration should be limited to carefully selected cases It cannot be done with impunity because of various serious sequelæ which may result.

5 Distortion and obstruction of the major *ducts, or obstruction of the pylorus or duodenum* in varying degree may follow cholecystectomy due to adhesions to the liver in the region of the gall-bladder bed These sequelæ can be minimized by accurate hemostasis and by covering the raw surface with peritoneum.

6. Wound separation or subsequent incisional hernia are frequent and serious complications of cholecystectomy Protracted vomiting as a postoperative symptom may be significant of a deep wound separation with incomplete high intestinal obstruction Adequate, painstaking suture of the incision and the use of ethylene or nitrous oxide as a basal anesthetic tend to decrease materially the incidence of incisional difficulties

7 Localized infection within the peritoneum may develop from contamination during a technically difficult procedure. Subphrenic abscess should be guarded against by protecting the space posterior to the gall bladder and common duct with gauze strips during operation on the biliary tract. Localization of the operative field by gauze pads and the generous use of suction limits the spread of infected material

8. Isolated conditions may arise as complications or sequelæ which will demand surgical attack

SURGICAL INDICATIONS FOR PEPTIC ULCER AND ITS SURGICAL MANAGEMENT

M E BLAHD, M D, F.A C S, CLEVELAND, OHIO

At present there are only three positive indications for the surgical treatment of peptic ulcer perforation, pyloric obstruction, and, occasionally, severe and uncontrollable hemorrhage More recent studies of the life cycle of peptic ulcer have definitely shown that patients having the deep penetrating type of ulcer can be permanently cured only by surgical intervention and that, therefore, this particular ulcer should be considered as a fourth positive surgical indication

Other surgical indications are only relative, in that they depend first upon whether or not the physician in charge of the patient is surgically minded, and second upon the individual desires of the patient It has long been believed that every peptic ulcer must first be subjected to medical treatment and, only when medical treatment has failed, dare there be consideration of surgery The time necessary to determine whether or not medical treatment has failed is variable In one of my patients who was finally referred for operation, it was more than 25 years Much has also been said about first giving medical treatment a fair trial, but just what constitutes such a fair trial is still vaguely defined As a prerequisite for the continuance of the present indications, it should first be ascertained if there is even a remote possibility of curing every peptic ulcer medically or if there are certain types of ulcer in which it can be determined in advance that medical treatment is doomed to failure In a recent address Boas of Berlin, talking about the surgical indications of peptic ulcer, made this significant statement "At the risk of being considered more surgically minded than the surgeon, not the number and length of medical cures but rather the character of the ulcer should be the determining factor" This seems to me to be the crux of the situation For, if we were able to say to our patient in advance that his ulcer can or cannot be cured medically, many medical failures may be avoided, early surgical treatment instituted, and the patient saved much in suffering and expense

The pathology of peptic ulcer is well understood The ever present[1] polypoid gastritis has long since been recognized It occurs both in gastric and duodenal ulcer, and, even if there were no other deterring agents, this inflammatory process itself would be sufficient to prevent healing This in spite of the fact that digestive ulcers have the same natural tendency to heal as ulcers situated elsewhere in the body Stomachs afflicted with polypoid gastritis are strangely reminiscent of the infected and hypertrophied urinary bladder which has been pounding against an obstructed outlet In both organs the hypertrophy pervades the entire wall, most marked, however, in the muscularis In the case of the obstructed bladder, the residual urine becomes foul and infected and gives rise to cystitis In the stomach the greatly thickened gastric wall causes one to surmise a similar stagnation of contents, resulting in polypoid gastritis When there is cicatricial contraction at the pylorus, the foregoing can be readily explained in its absence the *raison d'etre* is more difficult to understand It has been suggested[2] that a functional obstruction, a pylorospasm, occurring during the digestive act, might be equally efficacious At any rate, there is good reason to believe that polypoid gastritis is in some way the result of an obstructed pylorus either functional or organic This thought becomes more impressive when one pauses to consider that no other etiological factor has been discovered to explain this inflammatory phenomenon Carrying this line of reasoning to its natural conclusion the inference is that free unobstructed drainage should have a beneficial effect upon the inflammation Here again the obstructed bladder acts as a precedent Healing in peptic ulcer is accomplished by granulation, the granulations beginning at the base of the ulcer and gradually extending to the surface Unfortunately, however, in the lesions under consideration, the reparative process generally falls short of the mark, since the new and delicate granulations are infected and quickly destroyed by the omnipresent gastritis and duodenitis With each successive infection the ulcer, in terrace-like formation, pierces more deeply until it finally penetrates into a neighboring organ or perforates into the free abdominal cavity Obviously then a treatment to combat peptic ulcer successfully

[1] In a recent publication E Starr Judd and George W Waldron (Surg, Gynec & Obst 1934, 59 350) make the following statement And it is also realized that in this country we do not encounter the same type of lesion that the European surgeon has to contend with the ulcer with an associated extensive gastritis This has not been my experience Since even with the naked eye I was always able to find a high grade duodenitis and gastritis in all specimens removed These findings were substantiated microscopically by both Dr B S Kline, director of laboratories Mt. Sinai Hospital, Cleveland and Prof Howard Karsner

[2] This suggestion was first made to me by Dr B S Kline

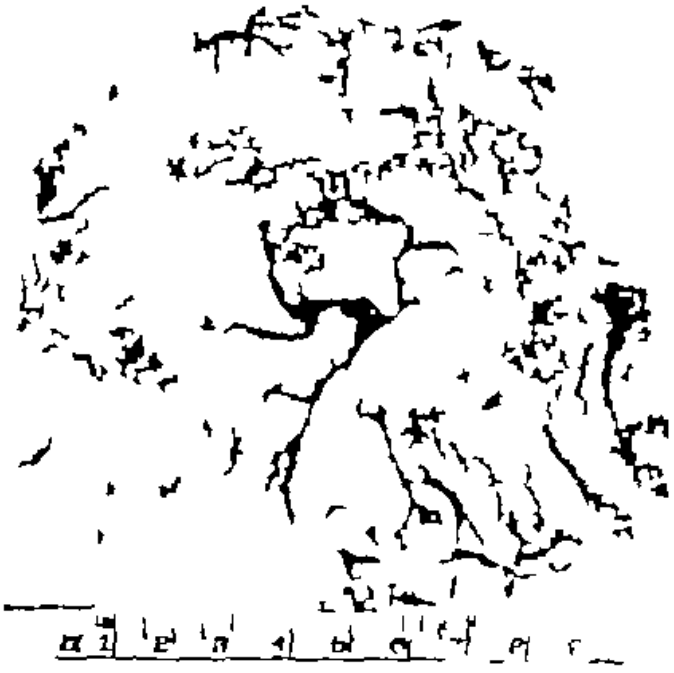

Fig 1a

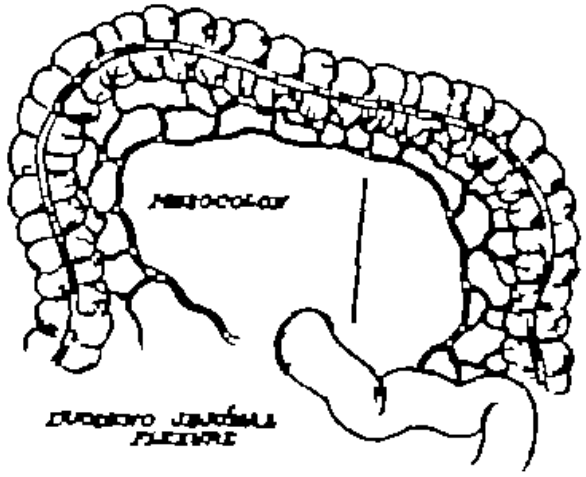

Fig c.

Fig 1b

Fig 1 a, Polypoid gastritis b, Penetrating gastric ulcer with barium filled crater c, Position of incision in transverse mesocolon This incision is made to the left of and line in an avascular area

must not only protect these delicate granulations but it must also cure the destructive gastritis and duodenitis, and eradicate the underlying pyloric obstruction, whether it be functional or organic In this respect it must be admitted that medical treatment has been a dismal failure Aside from these theoretical considerations, gastro-enterologists themselves, by publishing their final results, have brought striking proof of their inability to cope successfully with a large percentage of these ulcers.

Of the multitude of statistics available, those of Einhorn and Crohn, and those of David Smith, more than attest this fact. Einhorn and Crohn report 67 per cent cures after 1 year and only 22 per cent after 4 years. David Smith gives the immediate results in 214 cases treated between 1913–1922 as in Table I

Sooner or later most of these uncured patients seek relief at the hands of the surgeon, giving the surgeon the opportunity to determine that the vast majority of these failures were penetrating ulcers. On the other hand, statistics gathered from surgical clinics located in all parts of the world reveal upward of 90 per cent of permanent cures, with subtotal gastrectomy Furthermore, in penetrating ulcer medical treatment is far from safe, for experience has shown that not the superficial acute ulcer but rather the chronic, penetrating one is prone to perforate

This being the case how are we to diagnose ulcers which will not heal spontaneously or with medical treatment? Fortunately such ulcers are easily recognized on the roentgenographic film, since as has already been stated, they are penetrating in character and almost always contain a small amount of barium in the depths of the

TABLE I

	Cured Per cent	Dead Per cent
Immediate results		
Males	67	2
Females	76	5
Results 5 to 15 years later		
Males	29	19
Females	40	15

crater It is this crater formation which distinguishes these intractable ulcers from the more tractable superficial ones The latter cannot be seen roentgenographically and their presence may be surmised only by deformation of the roentgenographic contour of the stomach and duodenum Such superficial ulcers in contrast to the penetrating kind will usually heal spontaneously or with medical treatment If they do not, they soon become penetrating in character and join that large group of ulcers which can be cured only surgically

I have been so fortunate as to observe several patients who have for many years undergone medical treatment for penetrating ulcers Similar to other ulcer patients, they too had their periods of remission During these periods, when the ulcer crater was filled with newly formed granulations, the ulcer as such could not be demonstrated roentgenographically This led me to believe that a cure had been achieved Sooner or later, however, the polypoid gastritis and duodenitis reasserted itself and destroyed these newly formed granulations, and once again the ulcer was in full bloom, and could readily be seen fluoroscopically with a fleck of barium in the depth of its crater This cycle repeated itself many times During the remissions these unfortunate patients have the false sense of security in believing that their ulcers have been lastingly cured But, if the truth were known, they were verily standing on the brink of the precipice with that great medical catastrophe—perforated ulcer—constantly threatening them

Bearing in mind the inadequacy of medical treatment and its attending dangers in penetrating ulcers, I believe myself to be justified in stating that penetrating peptic ulcers must be considered as a fourth definite surgical indication

SUBTOTAL GASTRECTOMY

Subtotal gastrectomy for the cure of peptic ulcer secures upward of 90 per cent of permanent cures, and its mortality, when all factors are considered, is certainly no higher and probably lower than that of less extensive and less effective operations However, there are still so many experienced workers in this field who disagree with this

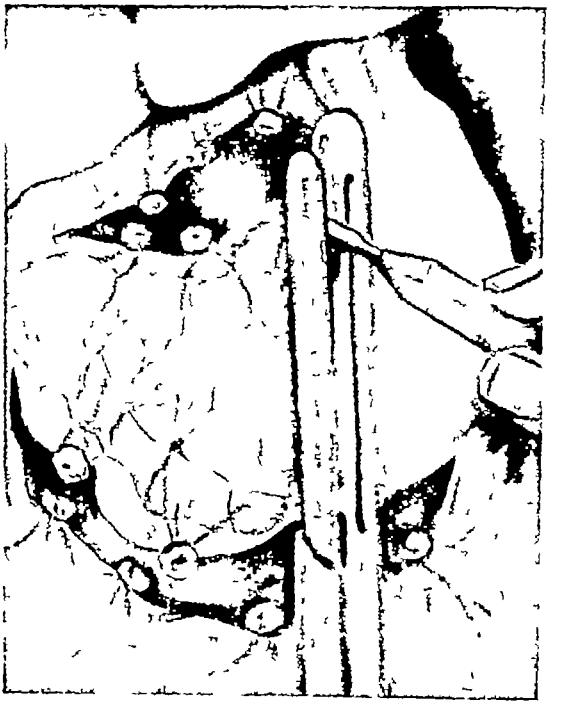

Fig 2 Stomach freed from its ligaments Mass ligatures for hemostasis Payr clamps applied at right angles to body axis

statement and who still believe in gastro-enterostomy, that it would be obviously unfair to dismiss gastro-enterostomy from consideration without first stating its pros and cons in comparison to subtotal gastrectomy The adherents of gastro-enterostomy claim that it will permanently cure 85 to 90 per cent of all peptic ulcers, with a death rate not in excess of ½ to 4 per cent These results, they say, are equally as good as those obtained with the more mutilating and dangerous subtotal gastrectomy If such brilliant results as set forth by the gastro-enterologists could be uniformly obtained by all surgeons, there would be no need of discussing or employing any other type of operation But the very fact that there is so much discussion of other operations gives evidence that all is not well in the case for gastro-enterostomy The following statistics relating to the cure of peptic ulcer with gastro-enterostomy are random selections from the literature, with the two exceptions of the figures emanating from the Mayo Clinic, and from Sherren's Clinic in London, which were purposely included, since these clinics are the leading exponents of the indirect method A total of 5,572 carefully followed up cases were studied (Table II)

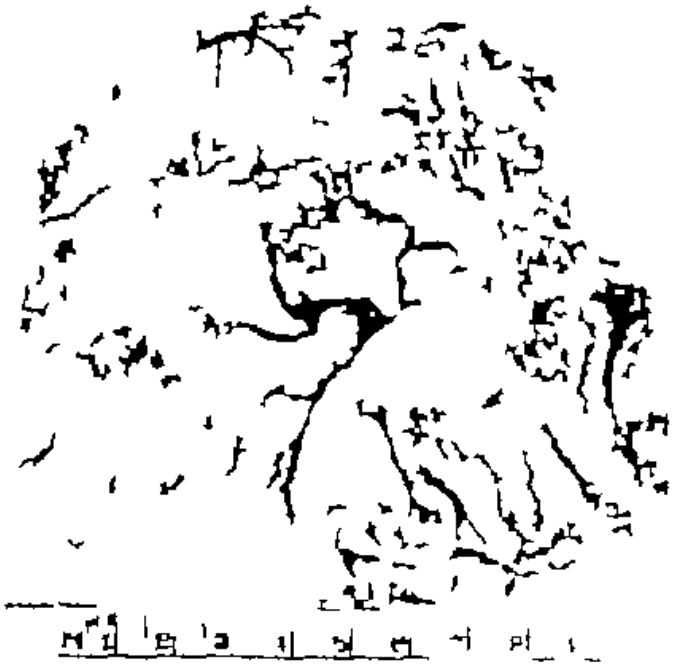

Fig 1

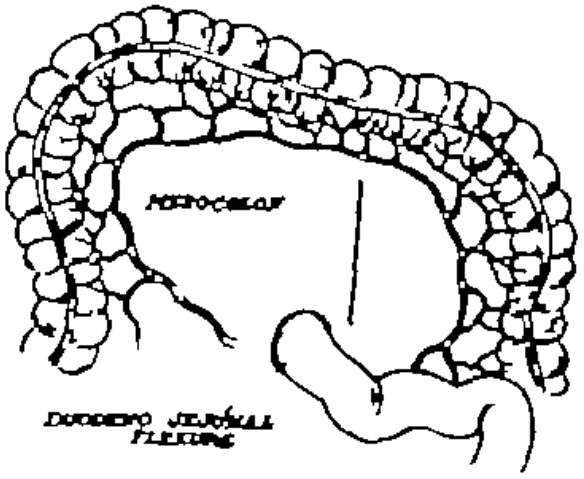

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TABLE II

Clinic	Cases	Cure per cent
Sherren	500	90
Metraux	210	90
Mayo	1000	88
Paterson	447	78
T Royster	64	76 4
Coffey	305	73 1
Hans Lehman	93	72
Solkov and Ilyin	580	69 3
Sawkoff	3-7	69
Tremont Smith and McIver	412	67 2
Gatewood	163	66 8
V Horwitz	17	64 7
J Hohlbaum	3-	56 2
P Clairmont	-80	56
Johns Hopkins	96	56
R Wanke	170	52 5
R Lewisohn	68	50
Schwartz	200	50
Schmieden	250	50
De Takats	370	50
Kaelin	70	47
	5,572	71 7

TABLE III—FIGURES OF THE BRITISH ULCER COMMISSION

	Cases	Deaths	Mortality Per cent
Duodenal ulcers	995	50	5
Pyloric ulcers	454	12	3 6
Gastric ulcers	538	48	8 9
Hour glass	65	8	12 3
	2,052	118	5 7

When this high secondary mortality is added to the initial death rate it is evident that the mortality of gastro enterostomy is considerably higher than is generally supposed The many reports at hand conclusively demonstrate that such complications as mentioned are only very rarely observed following the more extensive operation *Secondary mortality following the resection method is practically nil* In his own series, the author has seen not a remote complication following the resection method which was either directly or indirectly attributable to the original ulcer Without this high secondary mortality the death rate of the resection operation is certainly not higher than that of gastro-enterostomy if anything, it is considerably lower That the immediate mortality of resection is capable of further reduction is proved by the fact that von Haberer was able to operate upon 99 patients, consecutive cases, without a death, Gatewood, 30, and the author, 37

In leaning backward in an effort to be fair to the adherents of gastro-enterostomy, I have used the figures emanating from the Mayo Clinic as a standard for the mortality rate Not all clinics

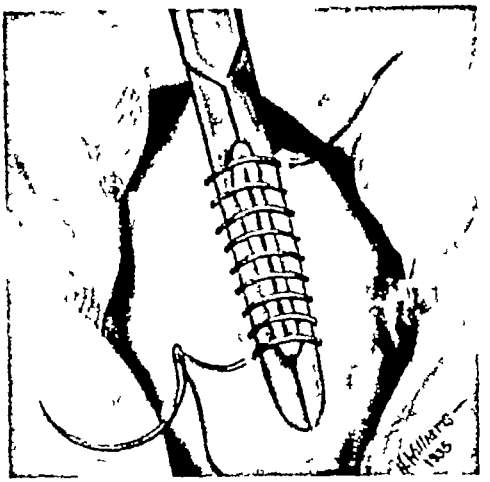

Fig. 5 Method of closing blind end of duodenum

have been able to match these statistics Moynihan, analyzing the 2,052 cases collected by the British Ulcer Commission in England (A Rendle Short), records an immediate mortality of 5 7 per cent, ½ per cent higher than that which obtains in the resection method

Jejunal ulcer, a condition unknown before the advent of gastro enterostomy, has been variously estimated as occurring in anywhere from 5 to 30 per cent of gastro-enterostomies (von Haberer Finsterer, Strauss, Lewisohn) That the frequency of this condition is generally underestimated is borne out by the fact that 4 such cases came under the writer's personal observation in the short period of 2 years The etiology of this condition, as that of peptic ulcer in general, is still considerably in doubt Nevertheless, its almost complete absence following the resection method gives rise to the thought that hydrochloric acid must play a very important rôle in the causation of this type of ulcer Several isolated instances of marginal ulcer have been reported following the Billroth II operation It is quite possible, however, that these were due to an incomplete resection Following the Billroth I, there is not a single authentic case (personal communication to the author from von Haberer)

As for the claim of pernicious anemia following the resection method, suffice it to say that literature records only a very limited number of such cases, in some of which it appears that the diagnosis has not been clearly established When this small series is compared to thousands of recorded cases of subtotal gastrectomy, of more than 5 years' duration, this alleged source of danger shrinks almost to the vanishing point

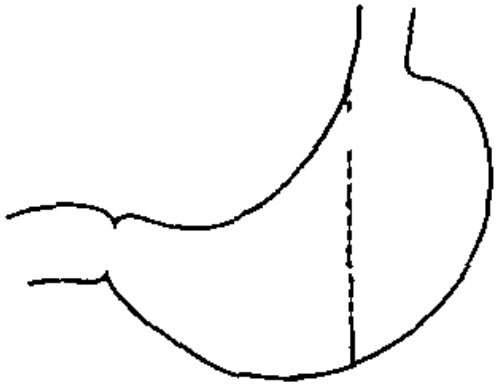

Fig 3 Severing stomach at right angles to body axis (Finsterer)

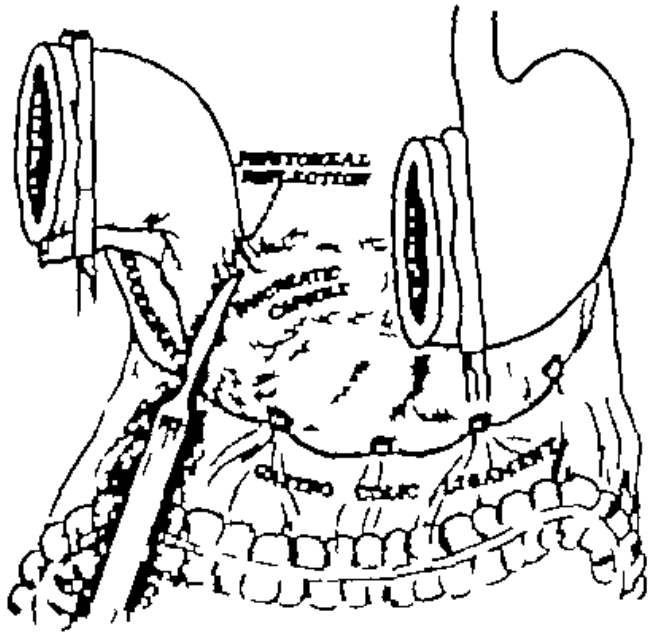

Fig 4 Dissection of duodenum according to Berg's method

Of these 5 572 cases, 71 7 per cent were reported as cures and partially satisfactory results The most striking information obtained from the foregoing figures is the wide divergence in percentage of cures—from 47 per cent by Kaelin to 90 per cent by the Sherren Clinic and Metraux This wide discrepancy is difficult to understand, and no attempt will be made to offer an explanation. It becomes more striking when the fact is taken into consideration that the above results were obtained in Class A clinics by competent surgeons using similar methods and similar technique This fact, however is clearly demonstrated—that uniformly good results are not obtained with the indirect method, and that at least 28 per cent of such operations completely fail to cure peptic ulcer

The analysis of the statistics of the *resection method* gives an entirely different picture. Here in contrast to the statistics on gastro-enterostomy the figures show a striking unanimity of results The percentage of cures ranges from 82 to 98 Included in these statistics are those of Von Haberer Moynihan, Finsterer Strauss, Berg, the writer and others. In the writer's own series, carefully followed by numerous personal contacts with the patients, the cures so far are upward of 90 per cent Before leaving the subject of cures, it might be well to mention the fact that following the resection method, no dietary regimen is necessary whereas on the other hand, the advocates of gastro-enterostomy insist upon continuous diet even after operation This in itself is a paradox, for if gastro-enterostomy had cured these patients, why the necessity of further diet?

MORTALITY RATE

The next consideration the mortality figures of these two operative types, can best be served by studying the death rate of large series of cases as reported by the leading exponents of the two methods For this purpose the writer has selected 2 229 gastro-enterostomies performed for both duodenal and gastric ulcer at the Mayo Clinic, and 3 122 partial gastric resections performed for the same illness at various clinics throughout the world

The Mayo series gave an immediate mortality from all causes of 4 5 per cent in 545 cases of gastric ulcer and 2 per cent in 1 684 cases of duodenal ulcer a combined mortality of 2 6 per cent

In 3 122 cases of gastric resection collected from 16 different clinics, there was a mortality of 5 76 per cent

On the surface it appears that the death rate of gastro-enterostomy is somewhat less than that of resection but only a slight scratching of the surface suffices to show the fallacy of this impression. Although the operative mortality for 2,229 gastro-enterostomies was only 2 6 per cent, there was an added mortality from all causes of 8 per cent in an average postoperative period of 3 5 years How many of these fatalities were due to ulcer disease is not stated in the report It is fair to assume however that a certain percentage of these individuals required secondary operation for either recurrent ulcer jejunal ulcer vicious circle hemorrhage or perforation That such secondary operations entail an immensely higher mortality is an established fact According to Clairmont, secondary operations have a death rate twice as great as primary operations and in the case of jejunal ulcer perforation and hemorrhage this may reach five to six times the initial rate

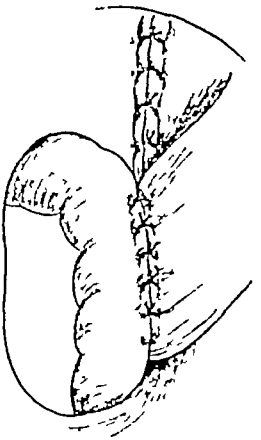

Fig 8 Anastomosis completed

taken to the operating room If necessary, a sedative, such as one of the barbituric acids, is given the previous evening

Selection of the anesthetic is of great importance, some form of regional anesthesia should be employed Three methods are available ligamentary (Finsterer), splanchnic, or subdural block. With the first method I have had no experience Splanchnic anesthesia, however, I have used in 28 cases, but believe it to be less reliable and no safer than subdural block For the past 6 years I have used spinal anesthesia routinely, supplementing with either gas and ether, or ether alone, for closure In my opinion regional anesthesia prevents surgical shock, produces more complete relaxation, and reduces to a minimum the postoperative complications of vomiting, gastric dilatation, intestinal distention, and pneumonia

The patient is placed on the operating table in the prone position, and the operative field is prepared in the usual manner The incision begins at the ensiform cartilage and is continued downward to either the right or the left of the umbilicus, according to the situation of the ulcer After the abdominal cavity is opened and the edges of the wound are protected with towels, a thorough exploration of the upper abdomen is performed The ulcer is sought for in systematic fashion by careful search from the duodenum to the cardia Identifying small ulcers on the posterior surface of the duodenum may offer great difficulties and unless unusual care is exercised, they may be overlooked The most reliable method of detecting a posterior ulcer is palpation These lesions will generally reveal their presence by an area of induration, part of which is represented by the raised indurated calloused edge of the ulcer

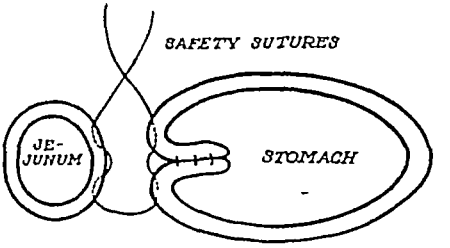

Fig 9 Transverse incision through stomach and jejunum, demonstrating position of safety sutures (Finsterer)

Stippling of the peritoneum in the neighborhood of the pylorus is a most unreliable sign, as even a slight trauma, such as is necessary in visualizing this portion of the alimentary tract, may produce a similar effect If the ulcer cannot be palpated, an attempt should be made to visualize it by transduodenal or transgastric inspection This step can be greatly facilitated by the insertion of an ordinary urethral endoscope or a Cameron light into the suspected area The finding of one ulcer does not end the search, as there may be multiple ulcers, one of which may be situated in the duodenum, the other on the lesser curvature of the stomach An enlarged lymph node will frequently reveal the hiding place of a gastric ulcer When resection is decided upon, the operation proceeds according to the situation of the ulcer I shall describe the procedure for duodenal ulcer, as the steps of this operation are the same as in gastric ulcer except that those steps which apply particularly to duodenal ulcer are omitted

With the left hand the transverse colon and omentum are withdrawn from the abdomen and made taut. The first portion of the jejunum, as it emerges from under the root of the mesentery at Treitz's ligament, is identified About 6 to 10 centimeters from Treitz's ligament, a silk suture is passed through the wall of the jejunum, marking its proximal end To the left of the spinal column, an avascular area is sought in the transverse mesocolon, through which a longitudinal incision 5 to 6 centimeters in length is made The edges of this are secured with silk sutures for future identification The suture marking the proximal end of the jejunum is now insinuated through the opening in the mesocolon and secured with a hemostat This step makes the jejunal loop, which is to be anastamosed to the stomach, available without the necessity of searching for it after the stomach has been opened

After the stomach has been made tense by an assistant, the index finger of the right hand of the operator is pushed through the middle of the les-

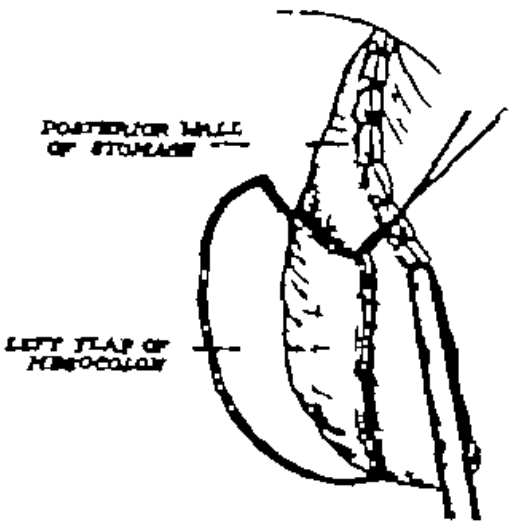

Fig 6 Upper half of remaining portion of stomach completely sutured (Hofmeister Finsterer method) left flap of mesocolon attached to the posterior stomach wall

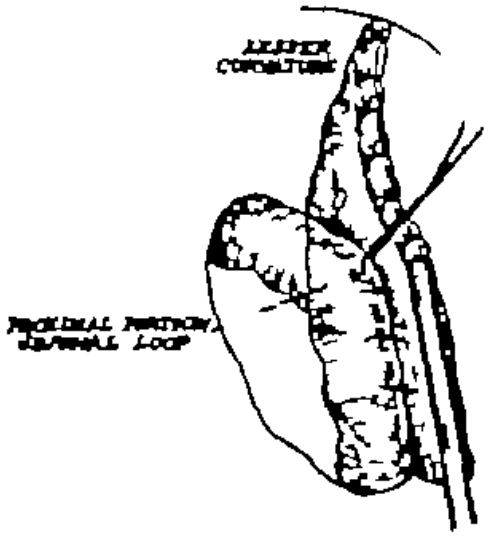

Fig 7 Jejunal loop sutured to posterior stomach wall Proximal portion of jejunal loop directed toward lesser curvature of the stomach

What has been said about gastro-enterostomy *applies for the most part to the various pyloroplasties.* Since these operations neither eradicate the underlying duodenitis and gastritis nor produce a reduction in the gastric acidity it is quite obvious that they cannot routinely cure duodenal ulcer for which they have been especially devised. If the stated facts concerning these operative procedures for dealing with peptic ulcer are impartially weighed *there can be only one answer* namely that, in the light of our present knowledge, subtotal gastrectomy is the only procedure which will consistently bring about a permanent cure for this disease

TECHNIQUE

The following description of the technique is given in considerable detail in the hope that the operation of subtotal gastrectomy may become standardized and more generally employed by both the gastric and the general surgeon The advantages of standardizing operative procedure are well illustrated by the operation of thyroidectomy Before thyroidectomy was standardized it was so dangerous that it was attempted only by the expert Today since it has been standardized, it is one of the safest operative procedures, and large series, with only an occasional death, are constantly reported I claim neither priority nor originality for the technique which I am about to describe, for I have merely taken the best points from the technique used by others, and only here and there added a slight modification of my own I do claim, however that all of these procedures have been thoroughly tried by me and that when they are carefully and painstakingly carried out, subtotal gastrectomy is just as safe as any other major abdominal operation.

Any patient who shows one or more of the surgical indications previously discussed is a candidate for this operation. Only those patients who have uncompensated heart lesions, severe nephritis, etc. are excepted Advanced age is not a contra-indication A number of our patients were *between 60 and 70 years of age and stood the* operation exceptionally well Neither need surgical shock, even in old patients, be feared It is a most rare complication This is proved by the fact that in only a very small number of cases was it necessary to perform a postoperative blood transfusion

Pre-operative treatment If the patient is seen during an acute exacerbation, he is put to bed and placed on a suitable diet until all symptoms have subsided The regimen which we most frequently use is the Sippey diet but any of the other well known diets answers equally well.

The immediate pre-operative treatment varies according to the case If there is food retention, gastric lavage with an old fashioned stomach tube is performed twice daily for 2 or 3 days a Levine tube is then inserted through the nostril for an additional 2 or 3 days until the fluid returns clear During this time the patient receives only sterile food

If there is no food retention, the patient receives a sterile diet for 24 hours and a gastric lavage the morning before the operation Pre-operative medication consists of either morphine or pantopon and atropine 1 hour before the patient is

bile ducts This step frees the portion of the duodenum which is to be removed, except for its attachment to the pancreas This attachment is released by a transverse incision of the peritoneal reflection between the duodenum and pancreas and, partly by sharp and partly by blunt dissection, the pancreas is dissected back beyond the point where the duodenum is to be severed During the dissection the gastroduodenal artery as it traverses across the pancreas may be met and must be ligated, also the numerous small pancreatic duodenal arteries and veins will require double ligation At the elected point, the duodenum is severed between two Payr's clamps by means of the high frequency current The distal clamp remains in position temporarily, and all protruding portions of the duodenum are seared away flush with the clamp The duodenum is closed as follows The handle of the Payr's clamp is held in the left hand Two or 3 millimeters below the crushing forceps on the posterior surface of the duodenum, at the border nearest the operator, a needle armed with No 2 chromic catgut is inserted in an upward direction to the depth of the submucosa, emerging immediately below the clamp The needle is crossed over to the opposite side of the duodenum and a similar stitch in a horizontal direction is placed adjacent to the clamp These horizontal stitches crossing from one side of the duodenum to the other are continued until the opposite border of the duodenum has been reached The last stitch is placed on the anterior surface of the duodenum, in similar manner to the first stitch except that the needle enters immediately below the clamp and emerges 2 or 3 millimeters farther down The two free ends of the suture are then grasped by the operator in either hand, continuous traction being made, while the first assistant withdraws the clamp from beneath the suture line This maneuver closes the duodenum and at the same time inverts the edges By means of the same suture, a continuous Lembert suture, beginning at the border where the first suture was completed, is inserted, inverting the first suture line A third row of interrupted silk Lembert sutures is placed above this Finally the sutured end of the duodenum is covered by a layer of fatty tissue taken from the immediate vicinity

The steps for closing the duodenum have been described in minute detail in order to impress my readers with the importance of this part of the operation Its greatest danger lurks in the closed blind end of the duodenum For, if leakage occurs at this point, not only may the entire purpose of the operation be defeated, but the outcome may be fatal Many other ways for closing the duodenum have been described, but after thorough trial of these methods, I believe the one which I have described to be the simplest, best, and safest. The upper half of the open proximal end of the stomach is now closed in two layers, the inner layer consisting of a hemostatic suture with Dulox, the outer layer of interrupted silk Lembert sutures The marker on the left border of the incision into the mesocolon is then located and this portion of the mesocolon is sutured by means of a few interrupted sutures to the posterior surface of the stomach close to its cut edge Next the marker on the proximal end of the jejunum is sought and the jejunum is anastomosed to the lower unsutured end of the stomach in such fashion that the proximal end of the jejunum is directed toward the lesser curvature of the stomach This anastomosis is performed in two layers in one of the usual ways of performing gastro-enterostomy After this the proximal end of the jejunum is attached by means of several mattress sutures to the superior portion of the stomach which was previously closed This step prevents kinking of the jejunum and protects the suture for closing the stomach at its most dangerous point. The right border of the incision in the mesocolon, upon which a marker has been placed, is sutured to the anterior surface of the stomach completely covering the anastomosis This brings the stoma submesenteric and protects the omental bursa from infection in the case of leakage Finally the abdomen is closed without drainage according to the preference of the operator When the ulcer has perforated into the pancreas, it frequently becomes necessary to permit the base of the ulcer to remain and then to insert a drain to this point

The postoperative treatment is most important and must be carried out with painstaking care There is considerable difference of opinion concerning the after-care Without entering into a discussion of methods employed by others, I shall briefly describe the method which I employ It has served me exceptionally well and I have no hesitancy in recommending it. Immediately after the patient is returned to his bed, he is placed in the shock position As soon as possible he is changed to a semi-sitting position and remains so during the entire convalescence For 5 days nothing is given by mouth During this time he receives daily by continuous venoclysis, about 3,000 cubic centimeters of 2 5 per cent glucose in normal saline He is frequently turned from one side to the other Under the direction of the nurse, he is made to take ten to twelve deep breaths every hour If he has a chronic bronchitis, he is

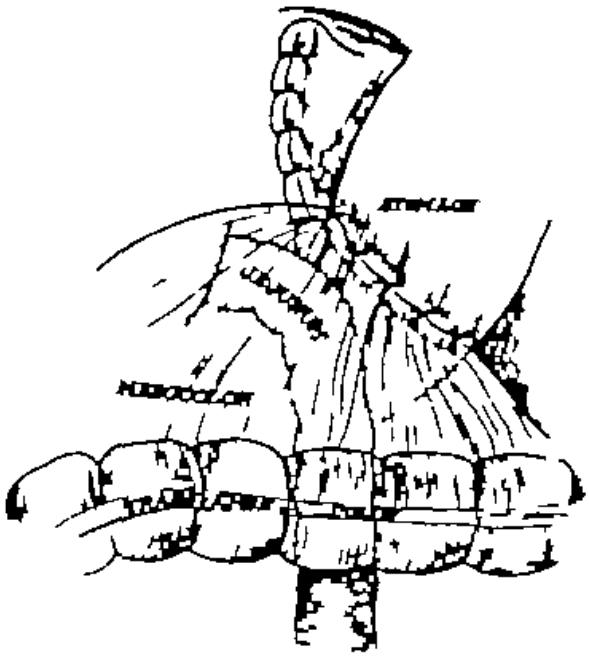

Fig Position right flap of mesocolon over anastomosis

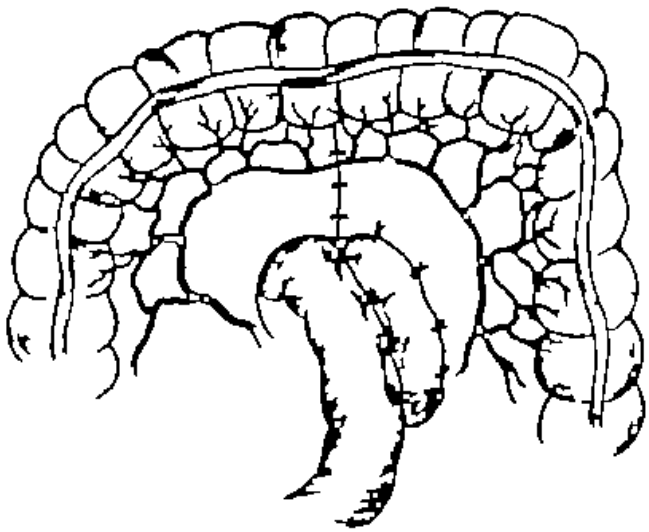

Fig Position of anastomosis below mesocolon

ser omentum. Proceeding first to the left and then to the right, the lesser omentum is severed between double ligatures without an attempt being made to isolate the gastric arteries. Generally three to four ligatures are sufficient The extreme *left portion of the omentum, roughly corresponding* to one-fourth of the stomach, is not severed, as this portion of the omentum is necessary to furnish blood for the remaining part of the stomach. On the right side, the severing of the omentum continues to the pylorus where it is discontinued, to be resumed later With the gloved hand the posterior layer of the mesocolon, which embraces the mid-colic artery is pushed from the posterior surface of the stomach, and the index finger is pushed through the greater omentum close to the greater curvature. The greater omentum is severed between double ligatures to the same extent as the lesser omentum It is preferable to place these ligatures within the arterial arcade. Even though the mid colic artery has apparently been pushed away care should be taken that it is not accidentally ligated and severed. This artery may be difficult to identify and if doubt exists as to its identity the transverse colon should be inspected for blanching before cutting the omentum at that particular point. The stomach is now *freed of its ligaments and ready to be resected*

The point at which the stomach is to be severed depends upon the desires of the individual operator at all events the entire pyloric antrum must be removed, otherwise the much desired reduction in the gastric acidity will not occur My own preference is to remove at least three-quarters of the stomach. The omental bursa is now protected by moist tapes and a straight intestinal clamp placed at right angles to the body axis, is put across the stomach at the point elected for resection A Payr's crushing clamp is placed in similar fashion 3 centimeters to the right. The stomach is then divided between these two clamps with the high frequency current. Severing the stomach at *right angles to the body axis places the future* stoma in the most advantageous position for complete and rapid emptying It also prevents regurgitation from the afferent jejunal loop. The two severed ends of the stomach are now protected with gauze sponges. At this point many operators prefer to complete the gastrojejunostomy in order that the operation may be interrupted should it become necessary This I believe to be a superfluous precaution as I have never found it necessary to complete the operation in two stages On *the other hand the primary dissection of the duo*denum permits the operator to make use of the relaxation afforded by the subdural block, before it wears off while the gastrojejunostomy can be painlessly and expeditiously performed without the aid of an anesthetic. The distal portion of the severed stomach is held in the operator's left hand and turned over to the right By employing light traction the unsevered ligaments of the duodenum and the pancreas with its peritoneal covering are brought into view This step first suggested by A. A *Berg greatly facilitates the subsequent dis*section. Next the duodenal ligaments are severed between double ligatures to a point about 1 to 1 5 centimeters beyond the ulcer In separating the ligaments on the superior border of the duodenum, care must be exercised not to injure the

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The priority of calling attention in America to the value of iodine in the treatment of exophthalmic goiter belongs to Plummer By carefully studying a large group of cases that had been benefited by the use of iodine as a pre-operative measure, Plummer placed its use in this disorder on a clinical basis The theoretical rational underlying this administration of iodine was that in exophthalmic goiter a dysthyroidism was present due to the production of an incompletely iodized thyroxin molecule To this incomplete product was attributed the power of entering into catabolic reactions faster than the normal, stable thyroxin molecule In changing the thyroxin molecule by adding the deficient iodine there occurred a lowering of the basal metabolic rate and improvement in the toxic manifestations In contrast to the exophthalmic type the so called toxic-adenomatous type was believed to be a hyperthyroidism due to an overproduction of the normal thyroxin molecule. Immediately following this work, numerous reports appeared in the American literature advocating the use of iodine as a pre-operative preparatory measure Due to the influence of Plummer these reports were singular in that they all advocated the pre-operative administration in the exophthalmic goiter and decried its use in the adenomatous thyroid In connection with the latter it was popularly believed that the administration of iodine might render the non-toxic ones toxic and aggravate the symptoms of the toxic adenomas The incorrectness of this concept was soon revealed in the reports of Graham, Starr, and Youmans and Kampmeier These authors demonstrated the similarity of response to iodine in both adenomatous and non-adenomatous goiters, and suggested that the exophthalmic goiter and toxic adenoma were but clinical variations of a single morbid disease Subsequently contradictory reports from various sources appeared in the literature At present, however, with the increasing literature (1, 2, 4, 5, 6, 7, 12, 13), there is a growing conception that only one type of hyperthyroidism exists, and that typical remissions with iodine in the majority of instances can be obtained in the nodular group as well as in the exophthalmic type

GENERAL CONSIDERATIONS

The purpose of this study was to determine the relative efficaciousness of pre-operative iodine therapy in hyperthyroidism associated with primary hyperplasia of the thyroid as compared to the hyperplastic glands containing nodules, the so called toxic adenomas

To add uniformity, 200 selected cases were chosen for this study Cases that had received previous iodine medication, X-ray or radium therapy, or that had had previous surgical intervention (polar ligations, hemi-thyroidectomy or subtotal thyroidectomy) were not included in this series Borderline cases, or cases presenting a question in diagnosis, were excluded Age, sex, intensity, or duration of symptoms played no rôle in the selection of cases

Since metabolic rate readings were to form a basic part of the study, only those patients having satisfactory metabolic rate determinations were chosen[2] After a satisfactory pre-iodine basal rate was obtained the preparation for operation was

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encouraged to cough and not to suppress it. In my opinion these simple precautions go far to prevent pulmonary complications. On the fifth day water in ounce doses is administered. The amount is gradually increased so that on the seventh day the patient receives fluids *ad libitum*. He is then given such foods as custards, junket, and ice cream. On about the eighth or ninth day pureed vegetables are added, followed by scraped beef, broiled meats, etc. On the twelfth to fourteenth day the patient receives the general hospital diet and generally at the end of 3 weeks he is discharged from the hospital with no restrictions whatever upon his food. Rarely is it necessary to administer morphine, as these patients seldom complain of pain If gastric distention occurs, drainage is instituted by a Levine tube Usually or almost always the convalescence is very smooth and in many instances the postoperative course is no more turbulent than that of an appendectomy for chronic appendicitis

In conclusion I wish to point out that this operation has been a source of utmost gratification to me for there are no more grateful patients than those who for years had been compelled to diet and then suddenly find themselves with a new lease on life able to eat anything and everything without the slightest discomfort. Each addition to the menu brings them increased happiness. They are like children with new toys. I might also add that, since I have given up gastro-enterostomy I no longer hesitate to enter the medical wards with the fear that one of my ulcer failures has come back to plague me.

I wish to express my gratitude to my surgical resident, Dr Elmer Good, for many valuable suggestions in the postoperative treatment

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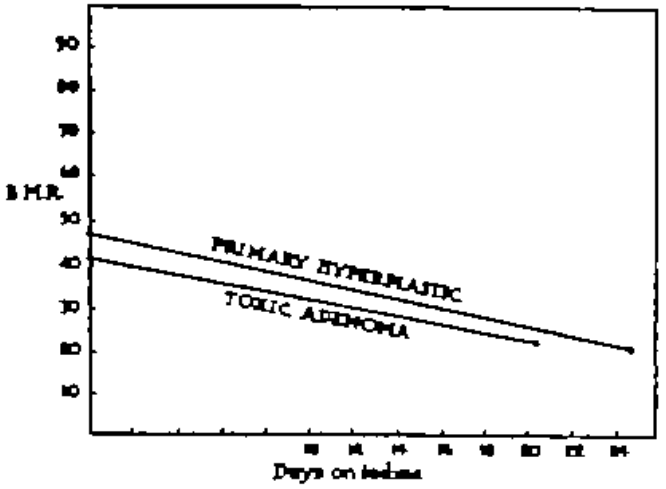

Chart 1 Average declivity of basal metabolic rate curves in each group

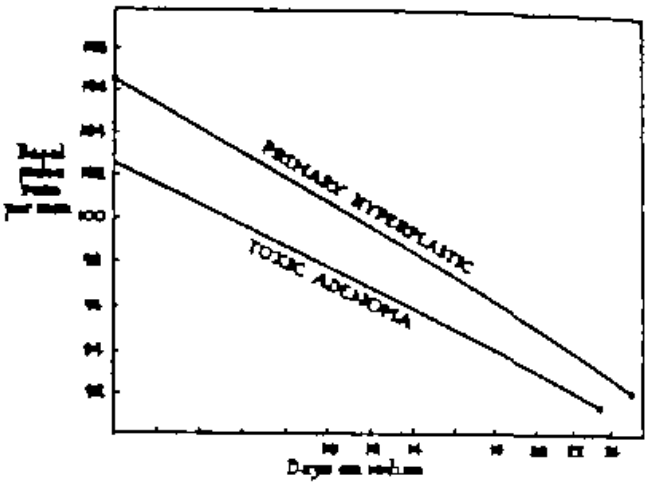

Chart Average declivity of pulse rate curves in each group

begun by administering iodine as Lugol's solution. This was given in doses of 30 or 45 minims (2 or 3. c cm) daily for 10 to 20 days In severe cases or occasionally because of social or economic conditions, it was necessary to continue the preoperative administration over a longer period of time. In the primary hyperplastic group the longest period of preliminary medication was 55 days in contrast to the shortest period of 9 days. The average was 25 3 days In the secondarily toxic (adenomatous) group, the longest period was 58 days, the shortest period 6 days or an average of 23.3 days. The remainder of this study was occupied in noting the comparative slowing of the pulse and gains in weight in each group.

BASAL METABOLIC RATES

The primary hyperplastic group consisted of 100 cases. The highest pre-iodine metabolic reading was +97 the lowest +22 or an average of +46.12 for the group The maximum decrease on iodine medication was 79 per cent Three cases proved to be iodine resistant and showed an average increase in the basal rate of 16 3 per cent In this connection it is interesting to note that even though these cases showed an increase in their basal rates, they gained in weight and were much improved by the preliminary medication The average lowest post-iodine rate was +20 91 The average reduction in the basal metabolic rate for the group was 25.21 per cent.

The group of toxic adenomata also consisted of 100 cases. The highest pre-iodine metabolic determination in this group was +92 the lowest +19 or an average of +41 24. The maximum decrease was 37 per cent. Three cases were iodine resistant showing an average increase of 7 per cent. These cases also showed clinical improvement and two of them gained in weight. The average lowest post-iodine rate was +23 78. The average reduction for the group was 17 46 per cent

From the foregoing, one is immediately impressed with the similarity of response to iodine in both groups This is graphically and more strikingly illustrated in Chart 1 which shows the average parallel declivity of the curves for each group

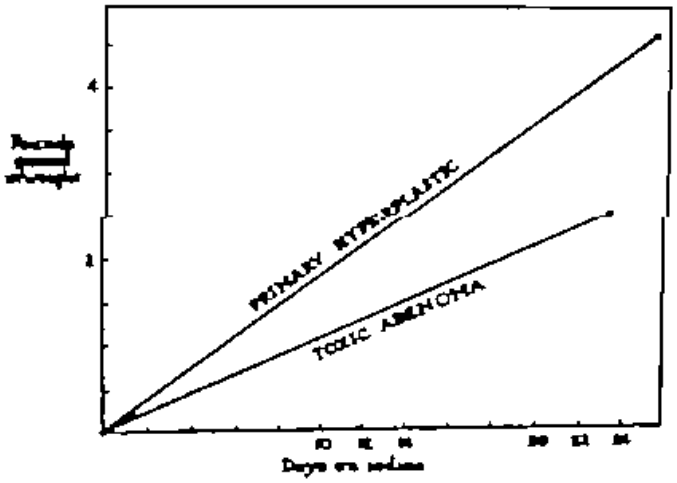

Chart 3 Average ascension of weight curves in each group

CHANGES IN PULSE AND WEIGHT

Similar changes were noted in the basal pulse rates. In the exophthalmic type the highest pre-iodine pulse was 143 the lowest 82 or an average of 106 3 beats per minute. The most marked decrease in the pulse rate was 42 beats per minute occurring in one case after 25 days medication Twelve cases showed an average increase of 9 6 beats per minute and in 5 cases the rate remained

unchanged The average diminution for the group was 14 5 beats per minute

In the adenomatous type, the greatest rise was to 130, the lowest to 78, or an average rise to 102 6 beats per minute In one case there was a decrease in the rate of 58 beats per minute after 21 days of Lugol's solution Twelve cases showed an average increase of 10 6 beats per minute In 4 cases the rate remained the same as before iodine was administered The average decrease in rate for the group was 11 3 beats per minute The above data reveals a marked similarity in response to iodine medication and is graphically illustrated in Chart 2

The differences in weight in each group were also similar following pre-operative medication The response though essentially the same in both the primary and secondary hyperplastic types, did not show the striking parallelism noted in the declivity of the pulse and basal metabolic rate curves In the exophthalmic type the most marked individual gain in weight was 17 pounds, the greatest individual loss 5 pounds Nine cases lost an average of 2 3 pounds In 5 of the cases the weight remained unchanged The average gain in weight for the group was 4 56 pounds

In the adenomatous type, the maximum individual gain was 18 pounds, the maximum individual loss 14 pounds In 16 cases there was an average loss of 3 4 pounds, and in 7 cases there was no change The average increase in weight for the adenomatous type was 2 63 pounds The comparative increase in weight for both types is illustrated in Chart 3

In both types of cases there was a striking general clinical improvement After the preliminary iodine medication, patients were less nervous and irritable They were either troubled less with heart consciousness or entirely relieved of this symptom In many cases their appetites improved and sleep was more restful Three cases of the adenomatous type and 1 case of the exophthalmic type failed to notice any amelioration of symptoms after preliminary iodine medication

SUMMARY

The response to pre-operative iodine medication was reviewed in 200 selected cases of exophthalmic and toxic adenomatous goiters The object was to study the comparative lowering of the basal metabolic rate, slowing of the pulse, and increase in weight, in each type of hyperplasia An almost parallel response was noted in the lowering of the basal metabolic and pulse rates The average ascension of the weight curves also showed a very similar response but the parallelism was not nearly so marked as in the declivity of the basal metabolism and pulse rate curves This favorable response, however, was not uniform in either group In each type, cases were noted in which the administration of iodine did not effect a depression of the basal metabolic rate, lower the pulse, or result in an increase in weight. All of the above data is therefore interpreted as signifying that the factors operating in producing hyperthyroidism is the same in both the primary (exophthalmic) and secondary (adenomatous) types of hyperplasia

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DUODENAL ULCER, SURGICAL TREATMENT

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A REVIEW of the development of the surgical treatment of *non-resectable* duodenal ulcer and a consideration of results may perhaps, aid in establishing basic principles in the treatment of *resectable* duodenal ulcer

Enterostomy which is done distal to the ulcer —jejunostomy—has not met with general acceptance.

Gastro-enterostomy (Fig 1) has been a favorite method, but as remote results and after effects of the resultant abnormal physiology have been more carefully analyzed a definite decline in its popularity has occurred.

Pyloric exclusion (Fig 2) was presented by Eisebberg as an improvement upon gastro-enterostomy This procedure was followed by such a high percentage of stomal or jejunal ulcers, however that it has been uniformly abandoned.

The next step in the pyloric exclusion operation included resection of parts of the stomach

Haberer at first in addition to the exclusion operation, removed the pylorus and the antrum (Fig 3) This method was not satisfactory so he improved his technique by doing besides the antropylorectomy a circumferential removal of the proximal, fundal, or acid secreting stomach wall (Fig 4)

Finsterer removed the proximal, or fundal, stomach (Fig 5) but allowed the distal stomach, antrum, and pylorus to remain.

The particular manner in which the gastro-intestinal continuity is re-established may or may not be an important detail when compared with the fundamental principles of the operation.

Of the various modifications of the Billroth I and II the Hofmeister Finsterer terminolateral anastomosis that aims to prevent retrograde filling of the duodenal stump seems to be meeting with favor (Fig 6)

The difference between the procedures of Haberer and of Finsterer is primarily in the removal (Haberer) and in the retention (Finsterer) of the antrum and pylorus.

Haberer and his followers deem it essential that the pylorus and the antrum be removed, because the secretion of the antrum is supposed to act as an important stimulant to the acid secreting cells located in the fundus. Edkins, years ago, promulgated such a theory, but it has not been accepted in various physiological laboratories and in the clinics of many surgeons.

Finsterer and his followers, on the other hand, allow the antrum and pylorus to remain, claiming their removal is unimportant. Finsterer and

Fig 1

Fig 2

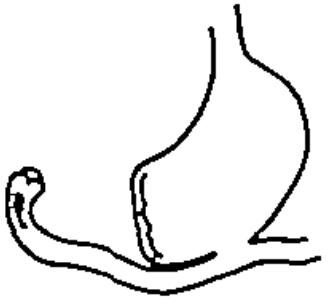

Fig 3

Fig 4

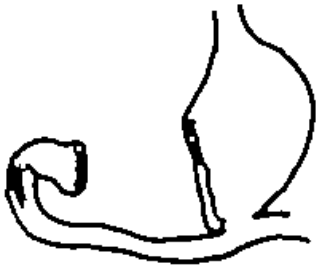

Fig 5

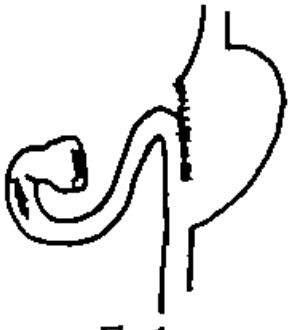

Fig 6

Figs 1 to 6 show the development of the surgical treatment of non resectable duodenal ulcer

Fig 1 Gastro-enterostomy

Fig 2 Gastro-enterostomy plus exclusion (Eisebberg)

Fig 3 Gastro-enterostomy plus resection of pylorus and antrum (Haberer).

Fig 4 Gastro-enterostomy plus resection of pylorus and antrum plus resection of part of proximal stomach,—partial or subtotal gastrectomy (Haberer)

Fig 5 Gastro-enterostomy plus resection of part of proximal stomach, but with retention of distal stomach (Finsterer).

Fig 6 Same as 5; but with Hofmeister Finsterer modification of Billroth II gastro-enterostomy (The many other modifications are not shown)

Fig 7 Sleeve resection is unsatisfactory

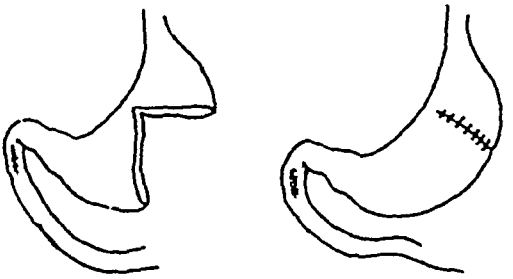

Fig 8 Partial fundusectomy preserves the direct motor continuity and diminishes the acid secreting area

Haberer agree upon the necessity of "adequate" removal of the acid secreting, proximal, fundal, stomach wall (only the cardiac third remaining)

And such a conclusion would seem to be supported by the increasing frequency of stomal or jejunal ulcers after gastrojejunostomy, and of the "intractable" cases in which recovery has not been achieved until two or three resections, for repeated recurrences, have removed most of the acid secreting fundus Such instances cause a surmise as to the result if the wide, or "adequate" fundal resection had been made at the first, instead of the last, operation

A review of these different operations and their underlying principles suggests the question If, in *non-resectable* duodenal ulcer, gastro-enterostomy, pyloric exclusion (Eiselsberg) and exclusion with resection of pylorus and antrum (Haberer) are not satisfactory, and, if exclusion with resection of pylorus and antrum and also circumferential resection of part of the fundus (Haberer) is more satisfactory, and if exclusion with circumferential resection of part of the fundus but *without* resection of pylorus and antrum (Finsterer) is equally satisfactory, why remove the pylorus and antrum in resectable duodenal ulcer?

The logical answer would seem to be that if removal of the antrum and pylorus is unnecessary in advanced, complicated, so called non-resectable ulcer, then their retention with removal of the fundus (with or without local excision of the ulcer) would be worthy of a trial in the earlier, simpler, more common resectable ulcer

The next question would logically be Can the resection of the fundus with retention of the antropylorus (Figs 5 and 6) be improved so as to preserve direct motor continuity? Sleeve resection (Fig 7) has been unsatisfactory "Partial fundusectomy" (Fig 8) does preserve the direct motor continuity and the important antropyloroduodenoneuromuscular mechanism and diminishes the acid secreting area

With organic pyloric obstruction an additional plastic operation would be indicated Without organic pyloric obstruction the ulcer might, or might not, be removed In either event operation should be followed by postoperative "medical management"

There are indications that hydrochloric acid is not the sole cause of peptic ulcer, but it is becoming recognized as a very important and constant factor among the fifty or more different explanations for the *chronicity* of the disease

The stomach seems to be a modified double organ, the proximal (fundus), concerned with acid secretion, and the distal (antrum-pylorus), having to do with alkali secretion and motor regulation Peptic ulcer is now considered as a physiological problem in which there is a lack of balance between an aggressive (acid) and a defensive (alkaline) factor

All of which calls for a reconsideration of so called "radical treatment," that is called radical because of the removal of the ulcer, alone, with the pylorus, or with the "ulcer-bearing area" Such measures might be considered as 'symptomatic," and the classification "radical" might be reserved for those methods in which an attempt is made to influence a supposed cause, or an important causative factor, such as hydrochloric acid

Treatment, heretofore, has been aimed chiefly at an increase in the defensive or protective forces by use of diets, antispasmodics, alkalis, demulcents, protein shock, operations, etc, etc The newer methods attempt to diminish the aggressive element by anti-secretagogues or by surgical minimization of acid secreting surfaces

There is a growing acceptance of the clinical fact that peptic ulcer is a general disease with a local lesion, that simple excision of the ulcer does not necessarily cure the disease, and that operative and non-operative measures should be not antagonistic but complemental

ORTHOPEDIC CONSIDERATIONS IN THE TREATMENT OF SPINA BIFIDA

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THE operative treatment of frank spina bifida in the newborn is of considerable interest to the neurological surgeon and in recent years clinical reports on this subject have frequently appeared in the literature Analyses of end-results by Cutler Coughlin, Penfield and Cone Kolodny, and Gross and Sachs have emphasized the life saving nature of early plastic repair of meningocele and myelomeningocele in this condition Paralyses and deformities of the lower extremities which have been present before operative treatment are however not usually benefited by this procedure and remain to be cared for by orthopedic methods. Flaccid and spastic muscle paralyses, deformed bones and joints, and more or less serious sensory trophic, and circulatory disturbances go to make up the sum of the orthopedic surgeon s problems Urinary and fecal incontinence with a predisposition to urinary tract infection, is also frequently found in these cases and constitutes a complicating factor in their treatment.

Similar problems are presented to the orthopedic surgeon in a somewhat larger group of cases in which deformities are found in association with an occult spina bifida. While it has been established that incomplete fusion of the laminæ of the lumbar and sacral vertebræ is normally very common in early childhood (Hintze, Steindler Neubert) the pathological significance of the persistence of these defects, in some cases showing incontinence of bladder and rectum or neuromuscular disturbances in the lower extremities, seems quite certain. In the clinical reports of Katzenstein, Cramer Brechot, Colby and others, pressure or traction upon the spinal cord and cauda equina, produced by fibrous bands and *myofibrolipomas* in association with vertebral clefts has produced a variety of disabilities. On the other hand, the studies of Fuchs indicate that a primary defect in development of the central nervous system, a myelodysplasia, may be associated with a persistent lumbosacral spina bifida occulta and give rise to congenital deformities of the lower extremities. *Deformities of the feet are* found frequently in childhood in conjunction with extensive defects in the laminæ of the lumbar and sacral vertebræ and clinically these malformations are distinct from other congenital types Congenital dislocations of the hip and spinal curvatures also frequently accompany vertebral defects, but the etiological relationship of the bifid spine to these deformities is not clear Urinary and fecal incontinence may be found in association with spina bifida occulta just as in cases of frank spina bifida with cystic myelocele, in which the nerve involvement is more obvious

A series of 90 cases of spina bifida treated at the Shriners Hospital of St. Louis, Missouri, from 1924 to 1935 has here been analyzed to define some of the variations in the clinical picture of this condition to be found in childhood and to evaluate the results obtained by standard orthopedic methods in the management of the problems which the condition presents. Of the 90 cases studied, 15 were cases of spina bifida with an associated herniation of the structures of the spinal canal upon which an early plastic operation had been done. The 75 other cases were to be classed as spina bifida occulta. Of this latter group, 39 showed defects in the spine in the lumbosacral region which were entirely lacking in signs and symptoms, and were discovered by X ray examination during the course of treatment for other conditions

Marked deformities and disabilities were characteristic of the group of cases of spina bifida with which a definite meningeal sac had been associated. All of these cases showed deformities of the feet, and these deformities were quite lacking in uniformity While the most common position of deformity was equinovarus, almost every other type of malformation was represented equinovalgus, equinovarus with cavus, calcaneovarus, calcaneovalgus, and simple equinus, calcaneus, cavus, varus, and valgus Frequently the deformities of the two feet were entirely different In 4 cases, a bilateral dislocation of the hip was found In 8 cases there was incontinence of urine and feces 2 were incontinent of urine only In 6 cases a tendency to hydrocephalus, was shown one patient being of subnormal mentality Eight showed diminution of sensation in the lower extremities *In 3 there was definite disturbance of* circulation in the legs In 4 cases trophic ulcers of buttocks and feet were noted. One patient admitted to the hospital for reconstructive work upon the feet was found to have a bilateral

hydronephrosis with hydro-ureter, and this patient died later of pyelonephritis Of interest in this case are the studies of Mertz and Smith, who have found that defects of the lumbosacral spine are associated not infrequently with paralysis of the vesical sphincter and obstructive dilatation of the upper urinary tract

Of a group of 36 patients showing deformities in association with a spina bifida occulta, 18 had malformations of the feet of various kinds Five patients showed congenital hip dislocations in addition to their deformed feet Nine other cases were found with congenital hip dislocations, unassociated with other deformities There were 7 cases of scoliosis 3 with a dorsal curvature, 4 with a double curve in the dorsolumbar region Four patients showed an incontinence of urine and feces, 2 were incontinent of urine only One of these patients, having an incomplete fusion of the sacral vertebræ, developed incontinence of bladder and rectum following an injury to his back at 11 years of age Three other cases are of more than ordinary interest a congenital malformation of the ear associated with a spina bifida of the cervical vertebræ, a congenital elevation of the scapula associated with a spina bifida involving the seventh cervical and first and second thoracic vertebræ, and a congenital absence of the neck of the femur associated with a lack of fusion of the first and second sacral segments of the spine In the entire group of cases showing deformities in association with a spina bifida occulta, no correlation between the size of the spinal defect (as shown by X-ray) and the degree of the deformity or disability could be determined

The treatment of the cases of spina bifida having from birth an obvious involvement of the central nervous system is summarized in Table I In general, this treatment has consisted of the correction of deformities of the lower extremities by manipulations, wedging plasters, the lengthening and transplantation of tendons, and the arthrodesis of joints Reduction of the four bilateral hip dislocations has not as yet been attempted Three of these cases have practically no muscle power in the lower extremities and have never walked In this group, wherever any degree of muscular strength existed in the lower extremities, orthopedic treatment improved the powers of locomotion Leg braces were frequently employed to maintain the correction of deformities of partially paralyzed extremities, and crutches were required in a number of cases

Cutler and Coughlin have emphasized the unfavorable prognosis in patients having incontinence of bladder and bowel, and the possibilities for relief of these individuals are few indeed Coffey's uretero-enterostomy may possibly be applicable in cases of urinary incontinence alone, but this operation can be of no help in cases of incontinence of both sphincters Transplantation of the gracilis muscle into the perineum to encircle the urethra may reinforce vesical sphincter action in selected cases of urinary incontinence (Deming, Player and Callander, Smith and Engel) Young's plastic operation upon the vesical sphincters may also be of use in certain instances According to Smith and Engel, the existence of some sensation of bladder filling or emptying is prerequisite for a good result when operations to reinforce sphincter control are performed In cases characterized by a marked urinary retention with overflow, presacral neurectomy, as described by Learmonth and Braasch, seems to be a promising procedure While this operation was first introduced to genito-urinary surgery in the treatment of the cord bladder produced by a postnatal nerve injury (transverse myelitis), it has now been successfully applied for the relief of urinary incontinence associated with congenital spinal defects C B Huggins of the University of Chicago has observed improvement in 4 of 5 incontinent spina bifida cases subjected to presacral neurectomy,[1] and Craig has reported a favorable result of the operation in the treatment of a case of urinary incontinence associated with a spina bifida occulta It should be noted that the experimental work of McCrae and MacDonald has indicated that the physiological basis for presacral neurectomy is in need of further investigation Reports thus far of the clinical results of presacral neurectomy are encouraging, however, and the operation would seem to be destined for a more extensive use in cases of spina bifida with incontinence

The problems involved in the handling of a case of spina bifida with marked nerve damage are illustrated by the following case (see Figs 1, 2, and 3)

G 85, M , 9 years Lumbosacral meningocele was present at birth. Plastic operations for the correction of this condition were performed after 12 hours The head increased in size abnormally during the first 3 months of life Plaster casts were applied for correction of deformities of feet at 1 year At 2 years of age, patient was seen at Shriners' Hospital for the first time On this occasion he showed a marked paralysis involving the lower extremities, hypesthesia of the lower extremities, bilateral dislocation of the hip, bilateral club feet, and incontinence of bladder and rectum The mentality was normal

Roentgenograms showed spina bifida involving the third, fourth, and fifth lumbar and all sacral vertebræ

[1]Personal communication

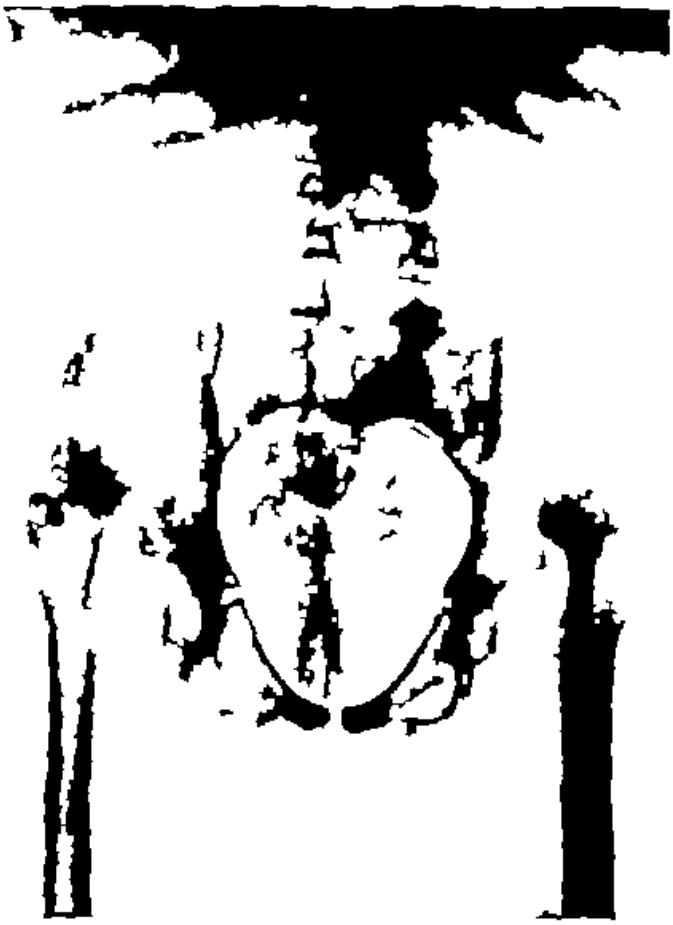

Fig Roentgenogram of Case G 85 showing laminal defects of third, fourth, and fifth lumbar and all sacral vertebræ

Treatment In 1927 manipulations of the feet with fixation in plaster were done In 1930, the right foot was manipulated under anesthesia, and a subcutaneous tenotomy of anterior tibial tendon was done Wedging plasters were tried, but were discontinued when pressure sores developed Right astragalectomy was carried out with lengthening of the heel cord Left astragalectomy was done Deformities of feet were corrected by these operations In 1933, patient was admitted, showing no motion in ankles but considerable equinovarus deformity Arthrodesis of both ankles was performed

Patient walked on crutches fairly well year after bilateral ankle arthrodesis, but still requires treatment for hip dislocations

Spina bifida occulta has long been considered to be a significant finding in certain neuromuscular affections of the lower extremity and in certain derangements of bladder and bowel action. Cases of urinary incontinence have been improved by laminectomy with the removal of fibrous bands from within the spinal canal (Katzenstein Brechot, Jacobovici, Urechia and Teposu, and Mertz) and deformities of the feet, and sensory and trophic disturbances usually appearing or becoming more marked in early adult life have been benefited by the removal of tumor

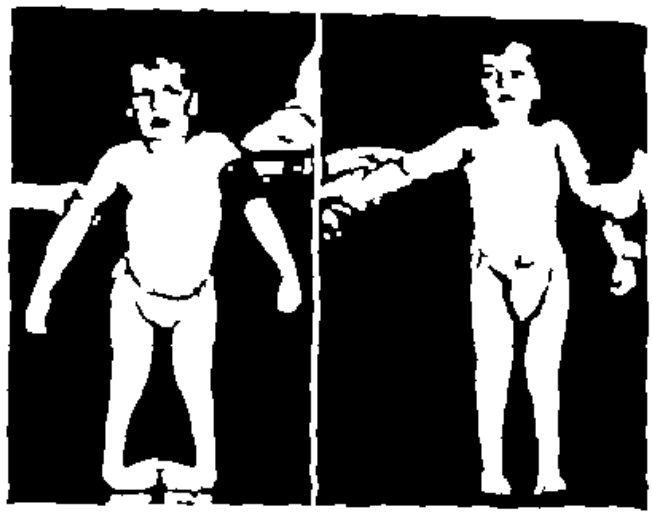

Fig 2, left Case G 85 before operative treatment
Fig 3. Case G 85 after bilateral astragalectomy and bilateral arthrodesis of the ankle joint

masses compromising the spinal cord or cauda equina (Jones, Sever Brickner Hackenbroch, Kochs, DeVries) All explorations of spinal defects have not been successful, however Indeed, Brickner Hackenbroch and Mertz have reported indifferent results in a considerable proportion of their cases In patients not benefited by laminectomy a primary defect in the spinal cord or an irreversible effect secondary to pressure has been assumed

Various deformities of the feet have been described in association with spina bifida occulta These are probably due, for the most part, to a muscular imbalance secondary to a congenital nerve defect. The club foot, claw foot, and flat foot are the more common of these deformities (Beck, Hackenbroch, Dittrich) It has been noted by Beck that deformities of the feet present from birth and associated with a persistent spinal cleft are more resistant to treatment than other congenital varieties. This resistance to treatment was certainly characteristic of the 18 cases of foot deformities considered in the present study (see Table II) Only 3 of these patients were treated with any degree of success by closed methods, and all the others required operative treatment, consisting in the main of arthrodeses of the tarsal joints and the lengthening and transplantation of tendons about the ankle. In a number of cases of this series, the presence of a spina bifida occulta was not discovered until the tendency of the deformities to recur suggested the advisability of an X ray examination of the spine.

The marked resistance to treatment of the foot deformities associated with spina bifida occulta is best explained on the basis of the muscular

Fig. 4. [illegible] H[illegible] showing lumbar defe[illegible] [illegible] vertebra.

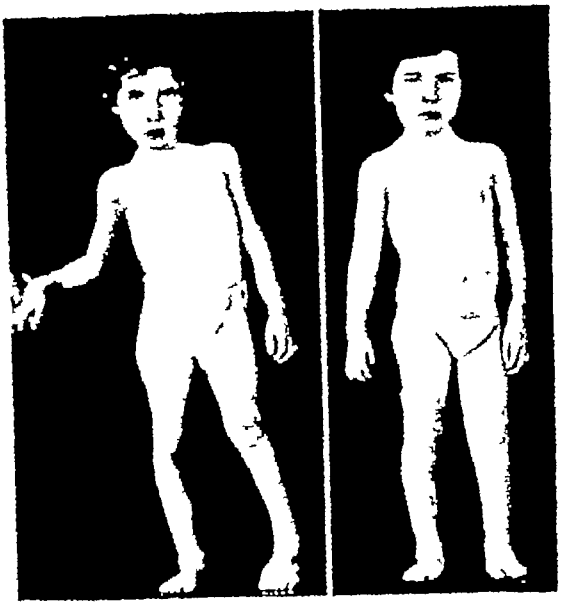

Fig. 5. left. Case H 130 before operative treatment.
Fig. 6. Case H 130 after lengthening of heel cord, triple arthrodesis, and tibial turn, left.

unbalance present in almost all cases. Stabilization of the foot, with shifting of tendons to balance more properly the forces acting upon the tarsus, constituted the plan of operative treatment which was most effective in the prevention of a recurrence of the old deformity.

The following case summaries illustrate the usual response of these patients to treatment.

H 130 [illegible] years (Fig. 4, 5, 6). Child was first seen at the age of [illegible]. She gave a history of club foot, left, since birth. She was treated with plasters in infancy without success.

Examination revealed the foot in equinovarus, with the canvas abnormally cold and cyanotic. Reflexes of the left lower extremity were not obtained. Mild flexion deformity of left knee was noted.

Treatment. In 1931 a wedging cast was applied to the knee to correct the flexion deformity. Three manipulations of left foot were carried out under anesthesia. Complete overcorrection of the foot deformity was accomplished by the treatment, but a recurrence was noted within a year. In 1933 full overcorrection was obtained by wedging plasters. A pressure sore developed at the base of the metatarsals on the sole of the foot during this treatment, but healing was readily accomplished by the application of alcohol dressings. Patient was discharged home walking well with an outside lift to her shoe. In 1934 examination revealed that the deformity had recurred within a year and on her third admission to the hospital, a spina bifida involving the third, fourth, and fifth lumbar and all the sacral vertebrae was found by X-ray. At this time, lengthening of the left heel cord with a triple arthrodesis and osteotomy of the tibia were performed. The foot was found to be maintained in good position 6 months after stabilization.

H 18 [illegible] years (Fig. 7, 8). History revealed presence of bilateral club foot since birth. No treatment had been given. Examination disclosed an equinovarus deformity on right, valgus deformity on left, dislocation of left hip. Over the spine in the lumbar region, was a pigmented mole about [illegible] centimeters in diameter. Sensation of both lower extremities was diminished. X-ray examination revealed a dislocation of the left hip, spina bifida of the third, fourth, and fifth lumbar vertebrae.

Treatment. In 1935, repeated manipulations of feet were carried out under anesthesia—lengthening of heel cord, left; section of peroneals, left; lengthening of anterior tibial, extensor digitorum communis, and peroneus tertius tendons, left. Chronic pyelitis complicated the hospital course at this time. In 1933 a wire was inserted through the lower left femur, and the head of the femur was pulled down opposite the acetabulum under 3 pounds of traction. Closed reduction of the dislocation was performed, followed by a supracondylar osteotomy. Open reduction of the hip dislocation became necessary later, when a redislocation occurred in walking. The hip was stable 2 years after operative procedures. The right foot was unstable, tending to turn into valgus in walking, left was held in fairly good position. Arthrodeses of tarsal joints of both feet are planned when child is older.

H 04 [illegible], 2 years. Pes equinovarus, left, has been present from birth. The condition was treated with plasters during the first year of life, and later the foot was manipulated regularly by the mother. Deformity was improved by these measures, but some residual equinus and inversion remained

Fig 7 Case I 18 showing deformities of feet before treatment

Fig 8 Roentgenogram of Case I 8 Laminal defects of third, fourth and fifth lumbar vertebræ Dislocation of left hip has been reduced

Treatment In 9 37 patient was admitted to the hospital One manipulation under anesthesia, followed by a wedging plaster seemed to correct the foot deformity very well Patient ore a brace on the left foot for 8 months after this correction A tendency to recur in the old deformity was noted, however 4 months after the brace was discarded An X-ray film at this time disclosed spina bifida involving the fifth lumbar and first sacral vertebræ The bony defects were of moderate size

Examination 3½ years after patient's discharge from hospital showed the left foot to be very stiff with tendency to inversion and adduction of the forefoot There is one inch shortening of the left lower extremity, with a knock knee deformity and marked atrophy of the musculature below the knee Stabilization of the foot, with an osteotomy of the tibia to correct the knock knee, will be performed when the child is older

On the whole the local operative treatment of the foot deformities associated with spina bifida occulta at Shriners' Hospital has yielded satisfactory results All cases considered in this study have not been followed to maturity to determine whether or not the operative correction of their deformities will be definitive Cramer Beck, and Hackenbroch have advocated exploratory laminectomy in cases of spina bifida occulta in which deformities recur in spite of local surgical treatment. It is possible that some of the cases reported here may show recurrences of their deformities later on, when, during the period of accelerated growth at puberty the damaging effect of bands or tumor masses within the spinal canal may be accentuated Deformities which are due to a primary defect of development of the central nervous system can reasonably be expected to remain corrected, however as the individual develops to maturity Laminectomy would seem to be a procedure to be reserved for cases showing recurrent deformity progressive muscular paralysis, or increasing sensory and trophic disturbances

The congenital dislocations of the hip associated with a spina bifida occulta have presented no special clinical features The 14 cases studied were treated by closed or open methods, as indicated by the character of the dislocation and the age of the patient and the results of treatment have been satisfactory Beck has concluded that the assumption of a causal relationship between a spina bifida occulta and an associated congenital hip dislocation is not justifiable It must be said that, from the evidence of this analysis, Beck's point of view cannot be controverted

The 7 cases of scoliosis of this series, with spina bifida occulta occurring in association, may also be said to be indistinguishable in their clinical characteristics from other types of idiopathic curvatures A causal relationship here between a

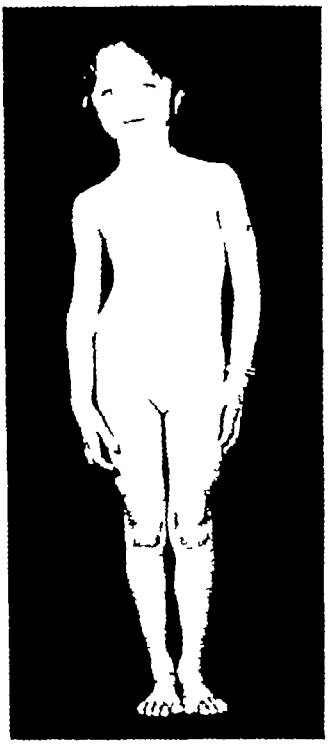

Fig 9 Case J 87 showing lumbodorsal scoliosis

spinal defect and a spinal curvature would seem plausible, but would be difficult to prove In this group of cases, the vertebral defects were found from the cervical spine to the sacrum, with the curvatures being dorsal and dorsolumbar There was no absolute regional agreement between the bifid vertebræ and the location of the scoliosis The cases were treated satisfactorily by jacket support, spinal fusion being reserved for treatment in certain selected cases Following is a typical case history of a patient of this group

J 87, F 5 years (Figs 9, 10) Curvature of spine was first noted by mother 11 months previous to admission There were no symptoms related to the spine. Treated by an osteopath with some benefit, according to mother

Examination revealed no abnormality of gait. Patient walked with shoulders squarely over pelvis with just a slight shift to the left Curvature of spine to the left was noted in mid-dorsal region No evidence of infantile paralysis General physical examination was negative

X-ray films revealed a left lumbosacral scoliosis, with the apex of the curve at the level of the eighth dorsal vertebra Sacralization of fifth lumbar vertebra was noted Spina bifida of fourth and fifth lumbar and all sacral vertebræ was present

Patient was instructed regarding exercise, and was fitted with a wedging plaster jacket Parents understand that a spinal fusion may be necessary, if conservative measures do not prevent further curvature

Fig 10 Roentgenogram of Case J 87 Laminal defects of fourth and fifth lumbar, and all sacral vertebræ, sacralization of fifth lumbar vertebra

The 6 cases of the present study showing dysfunction of the vesical sphincter in association with a spina bifida occulta have as yet received no treatment directed toward the relief of their incontinence In this type of case, laminectomy offers a better than 50 per cent chance of improvement (Mertz) In the treatment of patients whose symptoms are not relieved by such causal intervention, presacral neurectomy, and other operative procedures directed more particularly toward the reinforcement of sphincter control, remain as possibilities

SUMMARY

1 In this analysis is presented a summary of the orthopedic features of 15 cases of frank spina bifida in which patients have had a plastic operation upon the spinal defect early in life, and of 36 cases of spina bifida occulta found in association with deformities of the extremities and of the spine

TABLE I—CASES OF SPINA BIFIDA HAVING A CYSTIC TUMOR AT BIRTH

Patient Age Sex	Spinal defect	Deformities	Associated conditions	Treatment	Results
A 6 yr F	Lumbosacral (Plastic operation on gut day)	Foot fixed with compressions of legs and knees	Incontinent of urine Malformed sacrum on lower extremities Trophic ulcers of foot and buttocks	Section of hip flexors Contractures corrected by manipulations	Contractures improved within year after discharge Patient incapable of walking Prognosis poor
G 6 yr M	L and all sacral vertebrae (Plastic operation after hours)	Paralytic dislocations of hip Bilateral pes equinovarus	Incontinent of urine and feces, diminished sensation in lower extremities, trophic ulcers of feet	Manipulations of feet Walking on plasters Bilateral orthopedic surgery Bilateral orthoses of ankle joint	Feet in good position after year Walks with crutches Hip dislocations remain to be treated
G 18 mos F	Lumbosacral (Plastic operation at months)	Pes calcaneovarus, left Pes calcaneovalgus, right	Hydrocephalus Incontinent of urine and feces	Meningocele repaired Manipulation of feet Walking plasters	Walking well at years of age, except for tendency to invert feet, still incontinent, hydrocephalus not progressing
L 30 yr M	Lumbosacral (Plastic operation at weeks)	Bilateral pes calcaneovarus	Hydrocephalus Incontinent of urine and feces, diminished sensation in lower limbs	Patient fitted with crutches and braces	Stabilization of feet Transplant of anterior tibial tendon to mid tarsus, to be done later
L 24 mos M	Lumbosacral (Plastic operation early)	Bilateral pes varus	Hydrocephalus Diminished sensation in below knees	Manipulation of feet under anesthesia Walking plasters	Feet returned to varus deformity within year Stabilization not attempted for permanent correction
L 6 yr F	Lumbosacral (Plastic operation at months)	Pes equinovarus, right	Incontinent of urine and feces Ulcer of buttock	Walking plasters Transplant of anterior tibial tendon to outer tarsus	Excellent correction of
J 30 yr M	Lumbosacral (Plastic operation at days)	Bilateral pes calcaneovalgus Contractures of hips and knees, flaccid paralysis below knees	Incontinent of urine Trophic ulcers of buttocks	Section of dorsiflexors of foot, with bilateral double orthoses	Excellent result
K 11 M	Lumbosacral (Plastic operation at years)	Bilateral claw feet	Incontinent of urine and feces	Previous to years in Stimulation of first joint of the os calcis, bilateral After adolescence triple arthrodesis, plantar fasciotomy, and section of the posterior tibial tendon, bilateral	Good result after months
K 4 yr F	L Meningocele present	Legs flail below knees Muscle power diminished around hips, dislocation of both hips	Hydrocephalus Bilateral mentality on contraction of urine and feces diminished sensation in lower extremities	No operative treatment such could Parents forced to get child walker	Prognosis poor
D 44 yr F	All sacral vertebrae (Plastic operation in infancy)	Pes equinovarus, left Pes valgus, right, with flat foot varus	Bilateral hydroureteropyelonephrosis with hydroureter left cold, cystotic, and hypertrophic	Patient admitted to hospital for stabilization of feet	Patient died of peritonitis before operative treatment could be carried out
L 3 yr F	L L L L (Plastic operation at years)	Pes equinovarus marked	Hydrocephalus, slight	Repair of meningocele	Stabilization of feet to be carried out later
yrs M	L all S (Plastic operation at days)	Bilateral pes calcaneovalgus	Incontinent of urine and feces	No immediate operative treatment special indicated in view of age of patient	Patient was just returned to the hospital
yr	L (Plastic operation at weeks	Bilateral dislocations of hip, gluteal muscle weak, flexors of thighs contracted Flaccid paralysis below knees	Incontinent of urine and feces Slight hydrocephalus Left cold cystotic hypertrophic	Adduction of thighs corrected by osteotomy	Patient unable to walk Operative treatment deferred
yr M	L (Plastic operation at months)	Bilateral hip dislocations Bilateral pes equinovarus Knees partially anchylosed in recurvatum	Hydrocephalus Incontinent of urine and feces	Patient fitted with crutches	No operative treatment in detailed and child has learned to walk with crutches
yrs yr M	Lumbosacral (Plastic operation at months)	Pes valgus, right Pes equinovarus, left (mild)	Diminished sensation below knees feet cold	Previously at years of age had bilateral heel cord lengthening, with stabilization of right foot Restabilization of right foot not recommended	Gait at walking but operation

TABLE II—CASES SHOWING FOOT DEFORMITIES IN ASSOCIATION WITH SPINA BIFIDA OCCULTA

Patient Age (years) Sex	Spinal defect	Examination	Treatment	Remarks
A 92 - M	10D to 3L ++++	Fixed external rotation of hips and bilateral pes equinovalgus (Hypesthesia of saddle area feet and legs)	Osteotomy of femur, bilateral, with internal rotation of lower portion of shaft Triple heels for valgus deformities of feet	Patient improved
A 171 13 M	12D to 1S ++++	Dislocation of left hip Bilateral pes valgus	Closed reduction of hip dislocation Tenotomy of peroneal tendons bilateral Double arthrodesis, left	Patient walking well feet in good position after 2 years
B 89 4 F	5L ++ Spina bifida	Bilateral pes equinovarus contractures of knees and hips	Manipulations of feet Contractures corrected by traction and weighing plasters	Patient has never walked Incontinent of urine and feces Prognosis poor
B 193 12 F	1, 2S ++	Bilateral pes equinovarus	Bilateral lengthening of heel cord (Vulpius operation)	Excellent result
B 231 9 F	1, 2S ++	Bilateral pes valgus	Manipulation and fixation in plaster Bilateral lengthening of heel cords Double arthrodesis right Flat foot operation left	Feet in good position after 1 year
D 130 7 M	All sacral vertebrae ++++	Dislocation of both hips Bilateral pes equinovarus	Closed reduction of hip dislocations Repeated manipulations of feet Tenotomy of Achilles tendons Double arthrodesis, bilateral	It was necessary to restabilize feet 2 years after bilateral double arthrodesis
E 255 7 F	5L, 1S ++	Dislocation of both hips pes equinovarus left contracture of knee left with tibial torsion	Lengthening of heel cord, left Open reduction of both hip dislocations Subtrochanteric osteotomy, right Arthrodesis of left hip Triple arthrodesis, left Osteotomy of tibia and fibula left	Hips stable foot in good position after 1 year
G 32 10 F	1, 2S +	Bilateral pes cavus (most marked on right)	Steindler stripping of os calcis right Triple arthrodesis right	Good result after 4 years
H 139 7 F	3, 4, 5L All sacral +++	Pes equinovarus with some cavus, left Flexion of knee left (feet cold and cyanotic)	Manipulation and fixation of left foot in plaster Wedging cast to left knee Wedging plaster to foot Lengthening of heel cord left Triple arthrodesis left Osteotomy of left tibia for correction of torsion deformity	Foot in good position after 6 months
H 225 5 F	5L +	Bilateral pes equinovarus	Series of manipulations under anesthesia, supplemented by Kite wedging plasters	Good result after 2 years
I 77 9 F	5L to 3S +++	Bilateral pes equinovarus Flexion contractures of knees	Previous to admission Stabilization of feet *Osteotomy of femur, right* After admission Supracondylar osteotomy of femur, right Section of inner hamstrings right Erasion of knee, right	After 2 years, bending noted at the lower right femoral epiphysis with recurrence of flexion deformity Patient fitted with a brace to support knee
I 94 2 F	5L, 1S +	Pes varus left Shortening of left leg with genu valgum	Repeated manipulations Wedging plasters	After 2½ years still a tendency to inversion and adduction of forefoot Operative procedures indicated stabilization of foot, osteotomy of tibia.
I 256 4 F	4, 5L All sacral +++	Pes equinovarus right Pes calcaneovalgus left (Hypesthesia of feet and saddle area)	Wedging plasters to left foot, and manipulations under anesthesia	Patient walking well after 1 year; incontinent of urine and feces Removal of large lipoma overlying spina bifida recommended.
J 97 7 F	All lumbar and sacral vertebrae ++++	Flail lower extremities contractures of knees Bilateral pes equinus Dislocation of hip left	Deformities corrected by wedging plasters	Walking begun with braces and crutches Patient incontinent of urine and feces Prognosis poor
J 271 11 F	5L all sacral +++	Pes equinovarus right	Lengthening of heel cord triple arthrodesis	Tendency to recurrence noted after 1 year Transplant of anterior tibial tendon to mid tarsus to be done later

TABLE II —CASES SHOWING FOOT DEFORMITIES IN ASSOCIATION WITH SPINA BIFIDA OCCULTA —Continued

Patient Age (years) Sex	Spinal defect	Examination	Treatment	Remarks
K 11 D F	D to S ++++	Almost full left heavy monopedy contracture of left knee left hip marked by shortened foot in normally rotated Pes equinovarus with some varus, left	Lengthening of heel cord, left, triple arthrodesis, left. Osteotomy of tibia, left. Deformity of hip corrected by traction	Shortening of the extremity increases in this patient chief deformity Walks with left hip slow
J 8 J	++++	Dislocation of hip, left Pes equinovarus, right Pes valgus, left	Manipulation of foot under anesthesia Lengthening of heel cord, section of peroneals and dorsiflexors of ankle, left Open reduction of hip, left	Walking unaided after 2 years T knee stabilization of foot late
H 4 J F	L, all sacral ++++	Pes equinovarus, left Paralysis of dorsiflexors of toes, posterior tibial, and peroneals, left, with weakness of gastrocnemius	Stabilization of foot recommended	Operative treatment declined

2 Deformities of the feet of various types were found in both groups of cases. These deformities were particularly resistant to treatment, and usually required some form of operative correction Arthrodesis of the tarsal joints, and transplantation of the tendons about the ankle were the operations most frequently performed

3 Congenital dislocations of the hip joint were also found with both the occult and the frank types of spina bifida These dislocations showed no distinctive clinical features and were treated according to rules applicable to the handling of congenital hip dislocations in general

4 Seven cases of scoliosis were found with spina bifida occulta as a concomitant condition. These cases were indistinguishable in their clinical features from other idiopathic spinal curvatures, and were given no special treatment.

5 Incontinence of bladder and rectum, present since birth, was an important complicating factor in the group of spina bifida occulta cases as well as among the cases of repaired meningocele or myelomeningocele The present hopeless outlook for these cases of incontinence would seem to justify any operative procedure holding promise of symptomatic relief of the condition

6. Causal intervention as represented by exploratory laminectomy in cases of spina bifida occulta showing signs and symptoms, has not been attempted In cases absolutely refractory to local operative procedures, or in cases in which the signs and symptoms are definitely progressive and distressing this type of surgical treatment would seem to be indicated In the handling of spina bifida in childhood however the orthopedic surgeon deals chiefly with deformities and disturbances of function which have been present since birth and are relatively static Symptomatic improvement of these disabilities by local operative procedures is, therefore all that is generally required.

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EXTRA UTERINE PREGNANCY

An Analysis of Three Hundred Thirteen Cases from the Harlem Hospital

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THIS study represents an analysis of 313 cases of extra-uterine pregnancy admitted to the Harlem Hospital from March, 1917, to February 1934. For the past 4 years a special chart has been used to record these cases. By means of these charts, all the symptoms are minutely analyzed. Before the introduction of these charts, the histories were not taken so critically so that whenever symptoms are not specifically described they cannot be included in the analysis.

The incidence of extra-uterine pregnancy at Harlem Hospital for this 17 year period can be seen in Table I.

TABLE I.—INCIDENCE OF ECTOPIC PREGNANCIES

Year	Gynecological total admissions	Ectopic pregnancies	Per cent
1917	[illegible]	19	7
1918	*[illegible]	[illegible]	6 8
1919	[illegible]	18	6
1920	*[illegible]	16	4 9
1921	*[illegible]	5	5
1922	[illegible]	17	4 3
1923	[illegible]	64	3 6
1924	[illegible]	38	
1925	579	12	3
1926	[illegible]	14	6
1927	968	13	3
1928	731	11	7
1929	776	17	3
1930	784	19	6
1931	799	16	
1932	738	19	2 9
1933	527	14	3
1934	56 Jan. to March	3	8
Totals	[illegible]	313	3 49

Abortions, not included, were admitted to Obstetrical Service during these years

The incidence of extra-uterine pregnancy during the years 1917–1924 was much higher than it has been since. This is particularly true for the years 1917–1919. The incidence of extra-uterine pregnancies for the entire series per total number of gynecological admissions is 3 49 per cent. The incidence during 1917 was 7 2 per cent. Prior to 1917 the annual incidence was about 7 per cent

AGE GROUPS

In regard to the age, most of the patients were between 20 and 39 years of age, 170 were between 20 and 29, and 123 between 30 and 39 years In 11 cases the patients were in the second decade and in 9 cases in the fifth decade. The total number of cases was 313 of these, 174 were colored patients, 103 white patients, and in 36 the color was not specified (Table II)

TABLE II.—AGE GROUPS

	10–19 years	20–29 years	30–39 years	40–49 years	Totals
Colored	8	104	58		174
White	3	48	47	4	103
Unspecified		7	18		36
Total	11	170	123	9	313

ANATOMICAL DIVISIONS

In analyzing the cases, they have been studied on the basis of their anatomical location The subdivisions of the tube are as follows. Interstitial portion, or that part which traverses the uterine horn the isthmial portion, or the constricted medial third the ampullary portion, or the outer two-thirds of the tube. The cases of ovarian or tubo-ovarian pregnancies in which the tube is obviously involved, are included under the ampullary portion. Those cases with implantation of the placenta in the free peritoneal cavity are designated abdominal pregnancies. In this analysis, 4 such cases are included, all of which are secondary to ampullary implantations.

In this anatomical division there are 64 cases of ampullary abortion, 87 cases of ampullary rupture, 34 of isthmial rupture, 14 of interstitial rupture, 88 cases in which the site was not specified, 14 cases of unruptured ampullary gestation. There are also 5 cases in which the patients died without operation, 4 in which posterior colpotomy was performed, and 3 in which laparotomy was performed for pelvic abscesses due to infection of old hematoceles.

DEATHS

Out of the series of 313 cases there were 26 deaths (8 3 per cent), the greatest number occurring in the third decade, the period of greatest frequency (Table III)

TABLE III —DEATHS

		Under 20	20–29	30–39	40 plus
White	6	0	2	3	1
Colored	18	0	12	5	
Unspecified	2	0	1	1	
Total	26	0	15	9	1

The greatest number of deaths, 10 (11 2 per cent), occurred in the group in which the site of the gestation was not noted There were 6 deaths in 87 ruptured ampullary pregnancies (6 9 per cent), 3 deaths in 14 interstitial pregnancies (21 4 per cent), 1 death following ampullary abortion, 1 death following posterior colpotomy There were 5 deaths in which the patients were too ill to be operated upon or else died during induction of anesthesia The mortality rate for the series is 8 3 per cent (Table IV)

Of the 26 deaths, 10 patients died of shock shortly after the operation Four more died of delayed shock during the course of the next few days There were 5 patients who were moribund on admission and died without operation Two patients died of generalized peritonitis One of these was a secondary abdominal pregnancy and operation was carried out. The other patient was too ill to be operated upon Posterior colpotomy revealed blood and pus from an infected hematocele There was 1 death from adynamic ileus, 2 from pulmonary embolism, 1 from pneumonia, and 1 from sepsis This last patient lived for 1 year and 4 days following operation and developed multiple osteomyelitic foci Therefore, of the 26 deaths, 19 followed abdominal operations, which gives an operative mortality of 6 per cent An analysis of the mortality according to the anatomical location is taken up in Table IV

TABLE IV —MORTALITY

	Number of cases	Deaths	Percentage
Ampullary abortion	64	1	1 42
Ampullary rupture	87	6*	6 9
Isthmial rupture	34	0	0
Interstitial rupture	14	3	21 4
Rupture, site not specified	88	10*	11 3
Unruptured ampullary	14	0	0
Died unoperated upon	5	5	100
Posterior colpotomy	4	1	25
Laparotomy for pelvic abscess	3	0	0
Total	313	26	8 3

*Includes a case of secondary abdominal pregnancy

CORRECT PRE-OPERATIVE DIAGNOSIS

The correct pre-operative diagnosis was made in 45 of the 65 ampullary abortions (70 3 per cent), in 75 of 87 ampullary ruptures (86 2 per cent), in 29 of 34 isthmial ruptures (85 2 per cent), in 12 of 14 ruptured interstitial pregnancies (85 7 per cent), in 76 of 88 ruptured extra-uterine pregnancies, site not noted (86 3 per cent) In a series of 14 unruptured ampullary pregnancies, the correct pre-operative diagnosis was made 6 times, or 42 8 per cent. It is thus evident that in tubal rupture, the clinical picture is more apparent than it is in tubal abortions The correctness of pre-operative diagnosis is approximately 15 per cent higher in the former group In the unruptured ampullary pregnancies, the correct pre-operative diagnosis was made in 6 of 14 cases, or 42 8 per cent Three laparotomies were performed for pelvic abscesses and evidence of old ectopic pregnancies were found None of these were diagnosed correctly before operation Thus, of 304 laparotomies, 243 were correctly diagnosed, giving a percentage of 79 9 (Table V)

TABLE V —CORRECT PRE-OPERATIVE DIAGNOSIS

	Correct	Incorrect	Total	Percentage
Ampullary abortion	45	19	64	70 3
Ampullary rupture	75	12	87	86 2
Isthmial rupture	29	5	34	85 2
Interstitial rupture	12	1	14	85 7
Rupture—site not specified	76	22	88	86 3
Unruptured ampullary	6	8	14	42 8
Laparotomy for pelvic abscess	0	3	3	0
Total number of patients operated upon			304	
Total number of correct diagnoses			243	
Percentage of correct diagnoses				79 9

NUMBER OF PREVIOUS PREGNANCIES

The number of previous pregnancies, including abortions, was indicated in only 236 of the 313 cases There were 48 patients who were pregnant for the first time (Table VI)

TABLE VI.—NUMBER OF PREVIOUS PREGNANCIES INCLUDING ABORTIONS

None	[illegible]	[illegible]	[illegible]
	[illegible]		[illegible]
	[illegible]		[illegible]
2	[illegible]		[illegible]
	[illegible]	[illegible]	[illegible]

The incidence of ectopic pregnancies in nulliparous women is seen to be considerably lower than in the group in which the patients have been pregnant once or twice before.

DAYS BEFORE ONSET

The number of days before onset of symptoms following the last menstrual period is quite constant. Considering the time period in 10 day groups, it is thus seen that the greatest number of cases of ampullary abortion occurred in patients in the period between 40 and 49 days postmenstrual. The ectopic pregnancies which went on to rupture progressed for another 10 days before the onset of symptoms. This holds true for all groups except that in which the site of rupture is not mentioned. Although the date of the last menstrual period can not always be accurately ascertained, it can be seen from Table VII that these

TABLE VII.—NUMBER OF DAYS BEFORE ONSET OF SYMPTOMS

Days post-menstrual	Ampullary abortion	Ampullary rupture	Isthmial rupture	Interstitial rupture	Rupture—site not indicated	Current period
[illegible]	[illegible]				[illegible]	
[illegible]		[illegible]				
[illegible]					[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]		[illegible]	[illegible]		[illegible]	
[illegible]	[illegible]	[illegible]			[illegible]	
[illegible]		[illegible]			[illegible]	
[illegible]					[illegible]	
[illegible]						
[illegible]						
[illegible]					[illegible]	
Totals	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

cases fall into definite groups which give means which are constant enough to be significant.

There are 47 cases in which the acute picture (pain or bleeding) began before the onset of the next period. There were 14 ampullary abortions which occurred before the anticipated period, 12 ruptured ampullary pregnancies, 3 isthmial and 2 interstitial. Out of 24 unruptured ampullary pregnancies only 2 occurred in this manner. It is most unlikely that the last noted period was normal. Conception undoubtedly occurred before that time. It is important to bear in mind that even if a woman gives no history of menstrual irregularities or amenorrhea, she may not only be pregnant but may be concealing a ruptured ectopic pregnancy. This was so in 15 per cent of the cases in this series (Table VIII).

TABLE VIII.—CASES IN WHICH ACUTE PICTURE (PAIN OR BLEEDING) BEGAN BEFORE THE EXPECTED ONSET OF NEXT REGULAR PERIOD

		Per cent
Conceptional ampullary		
Ampullary abortion	[illegible]	
Ampullary rupture	[illegible]	
Isthmial rupture	[illegible]	
Interstitial rupture		
Rupture—site not specified	[illegible]	
Total	[illegible]	[illegible]

ANALYSIS OF SYMPTOMS

Onset. In 204 cases (65.2 per cent) a sudden onset of symptoms was noted. The highest incidence was observed in the moribund group (100 per cent) and ruptured interstitial group (85.7 per cent). A sudden onset occurred more frequently in the ruptured isthmial (79.4 per cent) than in the ruptured ampullary (75.8 per cent). The lowest incidence of acute onset occurred in the unruptured ampullary group (35.7 per cent) and in the ampullary abortion group (53.1 per cent) (Table IX).

Character of pain. Here again the same relationship between implantations at the uterine end of the tube and the character of the pain is noted (Table IX). The highest incidence of cases beginning with sharp pain is noted in the ruptured isthmial group (91.1 per cent). The ruptured interstitial group contained 2 cases that began with a gradual onset so these 2 cases lower the incidence to 85.7 per cent. The lowest incidence is again noted in the unruptured and ampullary abortion group. In 9 cases, a definite history of no pain was obtained. No pain was present in 4 of the 14 unruptured ampullary pregnancies. There was no pain in 1 case of ampullary rupture, in 2 cases of rupture site not noted and in 2 cases of ampullary abortions. In the most acute groups, moribund interstitial and isthmial—there were no cases without the symptom of pain. In the 9 cases in which pain was absent, the hypoesthetic factor must be considered. In such cases, one should attempt to elicit substitution symptoms.

TABLE IX.—ANALYSIS OF SYMPTOMS

	No of cases	Onset				Pain				Attacks			
		Sudden	Per cent	Gradual	Per cent	Sharp	Per cent	Dull	Per cent	Single	Per cent	Rep ted	Per cent
Ampullary abortion	64	34	53 1	30	46 9	47	73 4	17	26 5	6	9 3	58	90 6
Ampullary rupture	87	66	75 8	21	24 1	74	85 0	11	12 6	38	43 6	48	55 1
Isthmial rupture	34	27	79 4	6	17 6	31	91 1	2	5 8	16	47	16	47
Interstitial rupture	14	12	85 7	2	14 2	12	85 7	2	14 2	8	57 1	3	21 3
Rupture—site unknown	88	51	57 3	37	41 5	67	75 2	18	20 2	22	24 7	62	67 4
Unruptured	14	5	35 7	9	64 2	8	57 1	2	14 2	3	21 3	5	35 7
Died unoperated upon	5	5	100	0		5	100	0		5	100	0	
Posterior colpotomy	4	1	25	3	75	3	75	1	25	0		4	100
Laparotomy or pelvic abscess	3	3	100	0		3	100	0		0		3	100
Total number of cases	313	204		109		250		53		98		209	
Percentages		65 2		34 8		80 0		17 2		31 3		68 7	

TABLE X.—LOCATION AND RADIATION OF PAIN

	Total No of cases	Location						Radiation				
		Hypo-gastric	Per cent	Epi gastric	Per cent	Para umbilical	Per cent	Shoul ders	Back	Legs	Blad der	Rec tum
Ampullary abortion	64	57	87 5	7	10 9	2	3 1	3	8	7	13	10
Ampullary rupture	87	71	81 6	7	8	2	2	10	14	2	8	5
Isthmial rupture	34	29	85 2	3	8 8	1	2 9	3	6	1	6	6
Interstitial rupture	14	6	42 8	2	14 2			4	3			2
Rupture—site unknown	88	60	68 5	19	21 3			4	12	4	12	4
Unruptured ampullary	14	4	28 5	1	7 1					1	1	1
Died unoperated upon	5	3	60	2	40						1	1
Posterior colpotomy	4	3	75								3	
Laparotomy for pelvic abscess	3	3	100									
Totals		236		41		5		24	43	15	44	29
Percentages		75 4		13 0		1 4		8 0	14	4 2	14	9

Number of attacks of pain or bleeding The highest incidence of repeated attacks occurred in the ampullary abortion group, and the lowest in those that were ushered in with an acute onset (Table IX) In all the above, the gravity of the lesion increases the nearer the implantation is to the horn of the uterus It is fortunate, however, in that the incidence of these conditions decreases as the uterine horn is approached, the smallest number of ectopics being interstitial

Location and radiation of pain In 75 4 per cent of the cases, the pain was confined to the lower abdomen, the highest incidence being noted in the ampullary abortion group and the lowest in the interstitial group In only 24 cases was radiation of pain to the shoulders specifically noted (8 per cent) Pain radiating to the back was noted in 43 cases (14 per cent), to the legs in 15 cases (4 2 per cent) Bladder and rectal disturbances were noted in 44 and 29 cases respectively (14 per cent and 9 per cent) (Table X)

Faintness and syncope A history of faintness and syncope has always been considered of great diagnostic importance Actual syncope occurred in 205 cases (64 8 per cent), faintness in 59 cases (18 8 per cent) Combining these groups, these symptoms were noted in 264 cases (83 6 per cent) Syncope occurred in all the moribund unoperated upon patients In the patients operated upon, it was most frequently encountered in the group of ruptured ampullary pregnancies and least in the group of ampullary abortions It did not occur in any of the unruptured ampullary pregnancies In none of these cases had intraperitoneal hemorrhage occurred Although syncope was noted in only 5 of the 14 ruptured interstitial pregnancies, it is likely that these figures are incomplete due to the existing emergency The incidence of

faintness was higher in the isthmial rupture group (26.4 per cent) than in the ampullary rupture group (25.2 per cent) (Table XI)

TABLE XI.—HISTORY OF FAINTNESS AND SYNCOPE

	Totals	Present	Per cent	Syncope	Per cent
Ampullary abortion	64	3	[illegible]	14	[illegible]
Ampullary rupture	87	21	[illegible]	40	[illegible]
Isthmial rupture	34	9	[illegible]	12	[illegible]
Interstitial rupture	14		4	2	[illegible]
Rupture—site unknown	88	19	21 5	28	[illegible]
Unruptured ampullary	14		14		
Died unoperated upon	5			5	[illegible]
Posterior culpotomy	4		[illegible]		
Laparotomy for pelvic abscess	2				
Totals	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Vaginal bleeding Vaginal bleeding occurred in 230 cases (73.5 per cent) It was absent in 44 cases (14 per cent) Since these figures represent only 274 of 313 cases, it is significant that at least 14 per cent of all extra-uterine pregnancies are admitted without vaginal bleeding Of the cases presenting vaginal bleeding, the ampullary abortions and unruptured ampullary pregnancies have the highest incidence (90.6 per cent and 92 3 per cent) The lowest incidence occurred in the ruptured isthmial (61 7 per cent) and ruptured interstitial (50 per cent) groups. This is of great clinical significance. The patients who bleed seek medical aid earlier The patients who have no bleeding may progress further along in their pregnancies and therefore go on to rupture. The analysis of the number of days before the onset of symptoms substantiates this point. This was taken up in Table VII, in which the number of days postmenstrual was considered in 10 day groups. The greatest number of cases for a given 10 day group is considered the mean. The greatest number of cases of unruptured ampullary pregnancies occurred in the 30 to 40 day group. For the ampullary abortions, in the 40 to 50 day group, and for the ruptured ampullary isthmial, and interstitial abortions in the 50 to 60 day group. The group of tubal ruptures, site not indicated, falls in the 40 to 50 day period. Bleeding occurred only in 3 out of 5 moribund patients who died without operation (Table XII).

TABLE XII.—VAGINAL BLEEDING

	No. of cases	Present	Per cent	Absent	Per cent
Ampullary abortion	64	58	90 6	6	9 3
Ampullary rupture	87	76	84 3		6
Isthmial rupture	34	21	61 7	5	13 5
Interstitial rupture	14	7	50	5	35 7
Rupture—site unknown	88	67	75	11	12 5
Unruptured ampullary	14	13	92 3		7
Died unoperated upon	5	3	60		40
Posterior culpotomy			33		
Laparotomy for pelvic abscess			66 6		
Totals	313	230	73 5	44	14

Associated symptoms. Chills were noted in 10 ruptured ectopic gestations, 5 ampullary abortions, and 1 unruptured ampullary pregnancy Of the 10 ruptured ectopic gestations only 6 were definitely infected, the 4 others presented no clinical evidence to substantiate the presence of an infection. Two of the 5 patients with ampullary abortions had elevated temperatures. One unruptured ampullary pregnancy gave a history of chills and fever. Admission temperature was 100 degrees with a pulse of 90. The subsequent course did not indicate infection (Table XIII)

TABLE XIII.—ASSOCIATED SYMPTOMS

	No. of cases	Chills	Fever	Per cent	Vomiting	Per cent	Diarrhea
Ampullary abortion	64	5	2	3	14	21 5	
Ampullary rupture	87		4	4 5	41	48	
Isthmial rupture	34		2	5 8	16	47	
Interstitial rupture	14				7	50	
Rupture—site unknown	88	7		7 8	40	44	
Unruptured ampullary	14			7		14	
Died unoperated upon	5						
Posterior culpotomy	4					1	
Laparotomy for pelvic abscess	2					33 3	
Totals	313	10	3		133		
Percentages		3			42 8		17

A history of nausea was elicited from 23 patients. Vomiting was noted in 133 other cases, diarrhea once. Therefore of 313 cases, gastro-intestinal disturbances were noted in 157 cases (50 per cent) (Table XIII)

CONDITION ON ADMISSION

There were 223 patients admitted who were acutely ill (71.2 per cent) and 83 who were not (26.7 per cent) The ruptured interstitial pregnancies had the highest incidence (92 3 per cent) next to the moribund group (100 per cent) The

TABLE XIV—CONDITION ON ADMISSION

	No of cases	Acutely ill	Per cent	Not acutely ill	Per cent	Anemia			
						Sudden	Per cent	Gradual	Per cent
Ampullary abortion	64	33	51 5	31	48 4	15	23 4	45	70 2
Ampullary rupture	87	70	80 4	14	16	53	60 8	28	32
Isthmial rupture	34	30	88	3	8 8	21	61 6	11	32 3
Interstitial rupture	14	13	92 3	1	7 1	13	92 3	1	7 1
Rupture—site unknown	88	65	73	20	23 4	14	46	38	42 6
Unruptured ampullary	14	2	14 2	12	85 6				
Died unoperated upon	5	5	100			5	100		
Posterior colpotomy	4	2	50	2	50			3	75
Laparotomy for pelvic abscess	3	3	100					3	100
Totals		223		83		121		129	
Percentages		71 2		26 9		49 8		41 2	

TABLE XV—HEMOGLOBIN ON ADMISSION

	No of cases	20 per cent plus	30 per cent plus	40 per cent plus	50 per cent plus	60 per cent plus	70 per cent plus	80 per cent plus	90 per cent plus	Mean percentage
Ampullary abortion	64		1	1	7	6	22	12	3	70–79
Ampullary rupture	87	1	6	6	14	23	21	3	1	60–69
Isthmial rupture	34		1	8	3	7	8	4		40–49 70–79
Interstitial rupture	14		2	2	1	4	3	1		60–69
Rupture—site unknown	88	4	0	8	12	17	11	11	4	60–69
Unruptured	14					2	3	2	1	70–79
Died unoperated upon	5			1	3					50–59
Post colpotomy	4				1		2	1		
Laparotomy for pelvic abscess	3				1	1	1			

TABLE XVI—ABDOMINAL TENDERNESS

	No of cases	Generalized	Per cent	Localized	Per cent	Absent	Per cent	Pelvic Mass			
								Yes	Per cent	No	Per cent
Ampullary abortion	64	8	12 5	48	45 0	10	15 6	57	87 5	7	10 9
Ampullary rupture	87	17	19 5	57	65 5	6	6 7	65	74 7	19	26 8
Isthmial rupture	34	9	26 1	21	61 7	1	2 9	21	61 7	8	23 2
Interstitial rupture	14	6	42 8	8	57 1			7	50	6	42 8
Rupture—site unknown	88	14	15 7	69	77 5	4	44 9	70	78 6	13	14 6
Unruptured ampullary	14			11	78 4	2	14 2	13	92 8	1	7 1
Died unoperated upon	5		40	3	60			3	60	1	20
Posterior colpotomy	4	2	50	2	50			4	100		
Laparotomy for pelvic abscess	3	1	33 3	2	66 6			3	100		
Totals		59		221		23		243		55	
Percentages		18 8		71 2		7 5		77 9		17 5	

ruptured isthmial group had a higher incidence (88 per cent) than the ruptured ampullary group (80 4 per cent) The unruptured ampullary pregnancies showed the lowest incidence of acutely ill patients (14 2 per cent) and the ampullary abortions next (51 5 per cent) Only 158 of the 223

TABLE XVII—BLOOD IN PERITONEAL CAVITY

	Totals	Fresh	Per cent	Old	Per cent	None	Per cent
Ampullary abortions	4	30	78	12	20 7		
Ampullary rupture	87	79	90 8		4 8		
Isthmical rupture	34	30	88		5 8		
Interstitial rupture	24	24	100				
Rupture—site unknown	86	66	74	14	5 7		
Unruptured ampullary	4					4	100
Dead unruptured types	3						
Posterior colpotomy	4			4	100		
Laparotomy for pelvic abscess	3						
Totals		239		38		14	
Percentages		75 8				4 3	

acutely ill patients (51 1 per cent) presented the picture of sudden massive hemorrhage. Gradual anemia was noted in 129 cases (41 2 per cent) Again the sudden anemia is most frequently found *in the group of moribund and ruptured interstitial* pregnancies and least in the group of ampullary abortions (Table XIV)

Hemoglobin The hemoglobin determinations are analyzed in Table XV These figures are interesting but no attempt will be made to inter *pret them as the hemoglobin determination dur* ing or immediately following hemorrhage is not the true reading The hemoglobin was found to be highest in the group of unruptured ampullary pregnancies (no peritoneal hemorrhage) and in the ampullary abortions (slow bleeding)

The average hemoglobin for the entire series is found to fall in the 60 per cent to 70 per cent group On a service in which the average hemoglobin for all admissions is around 80 per cent or more it is very significant to find a hemoglobin of 60 per cent Even in the absence of accompanying symptoms, it is imperative that the etiology of such a degree of anemia should be ascertained.

Abdominal tenderness Abdominal tenderness was found to be localized in 221 cases (71 2 per cent) generalized in 59 (18.8 per cent) and absent in 23 (7 5 per cent) Generalized tenderness was most frequently found in the ruptured interstitial group, next in the moribund group and isthmial rupture group and least in the ampullary abortion group The highest incidence for localized tenderness was in the unruptured ampullary group It is thus seen that the less acute the clinical condition, the more likely that the tenderness will be localized and vice versa (Table XVI)

Presence of pelvic masses The presence of palpable pelvic masses was noted in 243 cases (77 9 per cent) No palpable masses were noted in 55 cases (17 5 per cent) The presence of a pelvic mass is lowest in the groups which present the most acute pictures and highest in the groups which have *the lowest incidence of acute symptoms* Walling off and hematocele formation occur most often when the hemorrhage is small in amount and repeated, and are least likely to occur in the presence of sudden massive hemorrhage. These processes will therefore accompany repeated attacks. *The incidence of repeated attacks is highest in the* ampullary abortion group. This observation that pelvic masses most commonly accompany the ampullary implantations is in keeping with the previous observation that the further the implantation is from the uterine horn the less acute the onset and clinical picture (Table XVI)

Blood in peritoneal cavity Fresh blood was found in 239 cases (75 8 per cent) old blood in 38 (12 1 per cent) No blood was found in the cases of unruptured ampullary pregnancy (Table XVII)

INTERESTING CASES

Previous extra-uterine pregnancies There were 8 cases in which the patient had a previous ectopic pregnancy 1 1 year before, 2 2 3 years before, and the others 3 4, 9 and 15 years previously There is 1 case in which the patient had an ectopic pregnancy in the stump left following an operation for a similar condition 4 years ago. The incidence is 2 56 per cent

Abdominal pregnancies. There were 4 secondary abdominal implantations, no primary cases. Two were advanced to almost the fifth month. Strangely enough, both of these were twin pregnancies. One case went to full term with a living baby The duration of the fourth was not noted The incidence of secondary abdominal pregnancy for this series is 1 28 per cent

Bilateral extra-uterine pregnancies There are 6 cases in which the diagnosis of bilateral extra-uterine pregnancy was made at the operating table. Gross examination revealed bilateral hematosalpinx In none of these cases, however, is there conclusive microscopic evidence to confirm the diagnosis It seems more likely that the condition noted was a tubal gestation in one tube with a hematosalpinx in the other

Other conditions The presence of an acute salpingitis in the same tube as the ectopic gestation was found in 2 recent cases It is possible that more have been overlooked In another case a tubal abortion was found in one tube and the other was the site of a ruptured pyosalpinx A ruptured ovarian cyst was found accompanying a tubal abortion on the opposite side A dermoid cyst was found in another case. In 3 cases, supravaginal hysterectomy was performed because of multiple myomata of the uterus

SUMMARY

1 An analysis of 313 cases of extra-uterine pregnancy is presented, the analysis being based upon the anatomical location of the implantation

2 The incidence of extra-uterine pregnancies (to the total number of gynecological admissions) is 3 49 per cent

3 The site of the implantation is found most frequently in the ampullary portion, less in the isthmial, and least frequently in the interstitial portion

4 The mortality rate for the series is 8 3 per cent Of the 26 deaths, 19 followed abdominal operation, thus giving an operative death rate of 6 per cent

5 The correct pre-operative diagnosis was made in 79 9 per cent of the cases

6 The number of days postmenstrual before the onset of symptoms is found to be greater for the patients who went on to rupture than for those in whom tubal abortion occurred

7 Fifteen per cent of the patients studied presented no history of amenorrhea at the time of admission

8 The severity of the clinical picture at the time of admission is directly related to the site of implantation, the nearer to the uterine horn the more sudden the onset and the more serious the effects

9 Abdominal pain was absent in 9 cases

10 Faintness, syncope or both were noted in 83 6 per cent of the cases

11 Vaginal bleeding was absent in 14 per cent of the cases in the isthmial and interstitial groups

12 Gastro-intestinal disturbances were noted in 50 per cent of the cases

Addendum From March 1, 1934, to June 15 1934, there have been 7 more extra-uterine pregnancies, 2 ampullary abortions 3 ampullary ruptures, 1 isthmial rupture, and 1 abdominal pregnancy The abdominal pregnancy was diagnosed before operation A five month fetus was removed No attempt was made to explore therefore it is not known whether or not this is a primary or secondary abdominal pregnancy The placenta was left *in situ* This patient recovered although she still has a discharging wound This case brings the number of abdominal pregnancies in this series to 5 The grand total of extra-uterine pregnancies is increased to 320

AN IMPROVED ANESTHETIC TECHNIQUE FOR GENERAL SURGERY[1]

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WITH a view of attempting to improve on the present surgical technique first, by abolishing psychic influences before operation second by securing a better brain block and greater relaxation during operation and third by diminishing gas and wound pain after operation, the following agents were used and the procedure as evolved was carried out more or less completely in over 300 patients In many cases, dilaudid was given solely for the relief of pain and as a sedative both in private and clinic cases by one of us (Fraser)

Reports by Alvarez of the Mayo Clinic and others prompted us to use dilaudid (dihydromorphinone hydrochloride) instead of morphine. Alvarez states "There is no question that in some cases dilaudid is an ideal analgesic Occasionally the appetite of patients is improved *and the appetite of others is not spoiled as much* as by morphine Every one who has used dilaudid seems to agree that it has practically no constipating effect It may be particularly useful in those many cases in which the patient with inoperable carcinoma must suffer tortures for several months

However Alvarez did not find the *effect* of dilaudid more *lasting* than that of morphine David states Dilaudid acts more rapidly but over a *shorter* period of time than does morphine.

As a long relief from pain is desirable we determined to use magnesium sulphate with the dilaudid Harmon states When the patient is given morphine in divided *doses in magnesium sulphate* solution prior to operation there is a greater postoperative comfort, less nausea and vomiting, and a decreased amount of morphine is used " Smythe states that with three hypodermic injections of 1 8 grain (8 milligrams) of morphine dissolved in 2 cubic centimeters of a 25 per cent solution of magnesium sulphate with 1/150 grain (0 4 milligram) of atropine added to the second dose at 20 minute intervals, one-third of the patients thus prepared did not require an analgesic after operation The patients go on an average four times as long after an operation before an analgesic is required than patients who were given morphine dissolved in *sterile water alone.*" (Average time with magnesium sulphate 15 hours and without 4 hours)

While a 50 per cent solution of magnesium sulphate has been used in many thousands of cases (3) successfully and Smythe has proved beyond doubt that a 25 per cent solution is satisfactory we determined on a 25 per cent solution for dilaudid. The synergism of magnesium sulphate is *even more striking than with morphine* (4). Both magnesium sulphate and dilaudid are analgesics—our usual dose is 1/48 grain and in some cases 1/96 grain Alvarez states "For one of my patients, the drug worked best when combined with a small dose of barbital. This tended to eliminate the nausea otherwise produced in her by a large dose " One of us (Gwathmey) had noted that nausea was diminished or entirely eliminated when a barbiturate was used preliminary to any inhalation anesthetic. We therefore gave all our patients a barbiturate—ipral sodium (ethylisopropylbarbituric acid) usually 2 tablets (8 grains)

Ether is unquestionably the safest and most relaxant of all anesthetics. The nausea and vomiting that is usual after inhalation ether is practically eliminated when mixed with oil and given per rectum. Two and one half ounces of ether in oil per rectum even when preceded by ipral and dilaudid magnesium, will never relax a patient to such an extent that an anesthetist is necessary before the patient is brought to the operating room (45 minutes) The supplement during operation is nitrous oxide and oxygen with an open mask and, as the operation is completed, oxygen and carbon dioxide. The final technique is. 2 hours before operation, 2 tablets per os of ipral *sodium (8 grains)* *One hour before operation,* first hypodermic intramuscularly of dilaudid, grains 1/48 in 25 per cent solution of magnesium sulphate repeat in 15 minutes *Now turn patient* on left side Sims position and give the following retention enema

Ether	2½ ounces
Olive oil	1½ ounces
Chlorbutanol	10 grains

For athletes, day laborers and alcoholics repeat the hypodermic, if necessary *The result of this* medication is a quiet sleep when patient is brought to the operating room Until this time no expert attention is necessary and was never given in any of our cases. This quiet sleep is converted into surgical anesthesia, and relaxation with an open mask (not the usual mask and bag), nitrous oxide (or ethylene) and oxygen being used—15 per cent

[1] Read at a meeting of the Metropolitan Hospital, January 20, 1926

to 50 per cent to which a 5 per cent vapor of ether may be added, if necessary The physiological balance between respiration and circulation is retained, with respiratory and circulatory rate normal This is not true of any form of inhalation anesthesia, unless heavily premedicated This sequence of hypnotics and analgesics followed by a mild inhalation anesthetic approaches the ideal The respiration, circulation and blood pressure would be only slightly altered by the necessary handling of a new-growth or important vessels and nerves but quickly returns to normal as operation approaches completion The patient is pink at all times The relaxation is second only to that obtained by spinal and, in some of our cases, was equally as good (Fraser) In one case the supplement was entirely oxygen and carbon dioxide, 6 per cent, at the end of the operation respiration was normal

With this method, all possible emergencies are provided for If loss of blood or unusual delay, a hypodermoclysis of normal saline, 500 to 1500 cubic centimeters, plus oxygen and carbon dioxide meets all requirements The patient is unquestionably safer and more comfortable afterward than with any other method we now have The long, quiet sleep after the operation is restful and life-saving, enabling the tissues to resume their normal relationship without painful reaction With this method and technique, the convalescence of the patient starts on the operating table and this is as it should be

ANALYSIS OF 40 CASES AT METROPOLITAN HOSPITAL

All statements of Alvarez in regard to dilaudid have been verified and concurred in by us (and also by Stroud) An analysis of 40 cases at the Metropolitan Hospital shows the following All operations were major multiple in type The average sleep after operation was 7 hours, with patient on right or left side requiring no expert supervision, lid reflex was active, breathing, natural In the surface cases, no supplement was needed In intra-abdominal cases a supplement was always used. The patients awoke in a pain free state and convalescence was quiet and uneventful The addition of a 25 per cent solution of magnesium sulphate (C P) definitely decreased the dosage of the dilaudid and prolonged its effect in our cases, as compared to those of others In a vast majority of cases the patients awoke without pain, nausea or vomiting Ether vomiting is a thing of the past

CONCLUSION

1 A definite prolongation of the effect of dilaudid is made by the addition of a 25 per cent solution of magnesium sulphate

2 The small amount of ether counteracts the depressing effect of dilaudid magnesium solution on the respiratory center

3 A comfortable relaxation with less shock and greater postoperative comfort occurs with this technique than with any procedure heretofore used

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EXPERIENCES WITH THE LATZKO CESAREAN SECTION[1]

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DEEPLY impressed with the enormous frequency with which craniotomy was done on the living child Frank among others, sought another approach to the fetus *in utero* when the abdominal method was indicated by a disproportion but contra indicated by the presence of a potential or frank intrapartum infection. In 1907 he devised the suprasymphyseal transperitoneal cesarean section extraperitonealizing the incision in the lower segment by sewing a mobilized flap of visceral peritoneum to the parietal peritoneum. With this method he hoped to avoid the usual complicating peritonitis and mortality which attended the classical section. To demonstrate the efficacy of his method he applied it in 13 frankly unclean cases. As a result he obtained 13 live babies and mothers, a striking contrast to the results previously obtained by the use of craniotomy on the living child which frequently was productive of permanent injury to the mother and the evident 100 per cent fetal mortality.

Sellheim carried this one step further and devised the purely extraperitoneal approach to the lower segment of the uterus through the space enclosed by the vesico-uterine reflection of peritoneum. He soon abandoned this method because of the marked frequency with which the bladder was injured and the peritoneal cavity opened. He then revived the Frank technique with some modifications.

In 1908, Latzko demonstrated a comparatively simple approach to the lower uterine segment in a purely extraperitoneal manner. This method was most practical when the patient had been in labor for some hours, at which time the lower uterine segment had been thinned out and the bladder made more mobile so that one gained easy access to the lower segment.

In this country the operation was introduced by Jellinghaus at the Lying In and the Nursery and Childs Hospitals in 1923. The experiences with the operation in these two institutions were reported by Steele and Burns.

In 1929, Dr. Meyer Rosensohn introduced the operation to the Bronx Hospital. The present report is based on a series of 19 cases on whom the operation was performed. The technique used was as follows. After the usual preparation of the abdomen and vulva the bladder was emptied, and then filled with 150-200 cubic centimeters of boric acid solution by means of an indwelling catheter. This procedure raises the bladder out of the pelvis and facilitates its mobilization. In addition, what is more important, it elevates the vesico-uterine fold of peritoneum, thus freeing it from the lower uterine segment.

A vertical incision is then made along the left paramedian line dividing the skin, fascia, and fibers of the left rectus muscle. The posterior layer of the sheath of the rectus muscle is now incised, great care being used to avoid the distended bladder which lies directly underneath. By means of blunt finger dissection, the left anterior surface of the bladder is then freed from the posterior surface of the posterior sheath of the rectus muscle. The fatty tissue surrounding the left lateral border of the bladder is now perforated with the blunt finger and dissected away until the anterior surface of the lower uterine segment is exposed. At this point it is well to give attention to a white band of tissue which extends from the upper end of the left lateral border of the bladder to the lateral pelvic wall. It can be readily observed pulling in the opposite direction when traction is made on the full bladder by means of a blunt retractor. This may be very carefully nicked thus exposing the peritoneal fold which is left intact, and pushed up out of the way by gentle blunt dissection. Extreme care with the disposal of what Latzko called, the ligamentum vesicale laterale, and the peritoneal fold, will invariably prevent opening of the peritoneal cavity. Most often one obtains sufficient exposure in a downward direction so that both these structures may be left intact. If the peritoneal cavity is opened, prompt suture with continuous plain catgut, before incising the uterus, will serve admirably to prevent any spill. Once more attention is turned to the bladder which is now completely separated from the lower uterine segment by blunt finger dissection. At this point, especially the operator should be warned of the danger of perforating the bladder as his finger approaches a very intimate attachment of the base of the bladder to the lower end of the lower uterine segment. Such an accident will occur even when the gentlest form of finger dissection is used, when the bladder is overdistended with too much fluid after it had already become devitalized by hours of incessant pounding from the hard unengaged head wedged in the brim of

[1] From the Obstetric Service of Dr. Meyer Rosensohn, Bronx Hospital.

the pelvis on the one hand, and the firm rigid bony inlet on the other One can avoid this complication by not overfilling the bladder, and in addition by incising the subvesical fascia which immediately overlies the lower uterine segment, by means of which a simple line of cleavage is obtained (Halban and Tandler do not consider this a real fascia, but rather a loose areolar tissue interspersed with smooth muscle fibers) The bladder is now emptied, by releasing the clamp from the indwelling catheter, and retracted to the right by a blunt retractor, the lower uterine segment being thus exposed If, up to this point, the procedure had been carried out correctly, neither the ureter nor uterine artery will have been exposed, and any danger to them will have been avoided The incision in the lower segment is now made as close to the median line as is possible without injuring the bladder We prefer starting this incision by making a small opening in the upper portion of the exposed lower segment with a scalpel, and completing it with a bandage scissors as far down as is compatible with the neighboring anatomy There is now sufficient room to complete delivery of the child with forceps Pituitrin may be given directly into the uterine wall, or hypodermically, as one desires, supplemented with an intramuscular ergot preparation, to aid and abet contraction of the uterus, thus preventing unforeseen hemorrhage

The lower angle of the wound in the uterine wall is now taken up with a No 2 chromic catgut suture This is done at this time because it gives one a landmark for the completion of the suture before the field of operation becomes inundated from the flow of blood following the manual removal of the placenta, which is now accomplished Up to the removal of the placenta, the operation has been a practically bloodless one, unless the operator has strayed from the midline (Case 19), and gone far out into the space between the leaves of the broad ligament where large sinuses have been opened A temporary hot gauze packing will control such bleeding, usually without any untoward difficulty The first row of the already anchored suture is now completed in a continuous fashion, and is followed by a continous chromic catgut No 2 Lembert suture of the overlying subvesical fascia and superficial layer of uterine muscle The bladder is now refilled in order to observe whether it had been injured in any way during the operation Such an injury can be detected from the evident escape of fluid at the site of the trauma A double or triple layer of fine chromic catgut suture, avoiding the mucosal layer of the bladder, is sufficient to re-establish the anatomical continuity of the bladder wall (This should be followed by the use of a permanent catheter, the drainage being continuous for the first 4 days, then interposing periods of non-drainage in ever increasing duration until the tenth to the fourteenth day when the catheter can be removed) The lateral border of the bladder is now allowed to return to its normal position after it had been again emptied A cigarette drain is interposed between the uterine wound and the bladder The mobilized bladder may or may not be anchored to the posterior sheath of the rectus muscle by one or two interrupted plain catgut sutures Experience has taught us that the anchorage of the bladder is not entirely essential

CASE REPORTS

CASE 1 A primipara at term, showed no appreciable dilatation of the cervix after 6 hours of active labor Three vaginal examinations had been made in the patient's home The indications for operation were a flat pelvis, unengaged head after 48 hours of ruptured membranes, fetal distress—rate varying from 130–180, irregular Mother's temperature at time of operation was 100 4 degrees The peritoneum was opened and promptly sutured The puerperium was complicated by exudate in the left broad ligament, foul purulent lochia, and edema of the vulva due to lymphatic obstruction Fever ranged as high as 102 8 degrees with temperature returning to normal on the twenty first day Patient was discharged cured on the twenty fifth day, with a living baby weighing 6 pounds 12 ounces

CASE 2 A primipara at term Membranes had been ruptured for 8 hours, she had been 46 hours in active labor, with head unengaged and cervix fully dilated Three vaginal examinations had been done in the hospital The fetal heart could not be heard for the last hour of labor An attempt at craniotomy was a failure due to tetanic spasm of the uterus. Indications for operation were flat pelvis, unsuccessful craniotomy, impending rupture of the uterus. Mother's temperature at time of operation was 102 6 degrees Catheterization before operation, was productive of bloody urine, although there was no difficulty in filling the bladder The bladder, tested at operation, revealed no evident injury The puerperium was complicated by purulent discharge from the abdominal incision, and a vesicovaginal fistula which appeared on the sixth day Temperature returned to normal on the ninth day, and patient was discharged on the twenty second day The craniotomized baby weighed 6 pounds plus Patient refused operation for fistula at a later date

CASE 3 A primipara, at term, with cervix two fingers dilated Two vaginal examinations had been done in the hospital Labor was complicated by pre-eclampsia Indications for operation were flat pelvis, unengaged head after 36 hours of ruptured membranes with 30 hours of active labor, temperature 101 8 degrees The puerperium was complicated by purulent discharge from the abdominal wound and foul lochia Temperature returned to normal on the thirteenth day, and patient was discharged cured on the sixteenth day Living baby weighing 8 pounds 9 ounces was delivered

CASE 4 A primipara, at term, with cervix four fingers dilated Previous history showed chronic pyelitis Indica

tions for operation were flat pelvis, unengaged head after 30 hours of ruptured membranes and 30 hours of active labor Two vaginal examinations were done in the hospital Temperature at time of operation was 101 4 degrees The puerperium was complicated by pyuria The temperature returned to normal on the seventh day and patient was discharged cured on the eighteenth day The wound healed by primary intention A living baby weighing 7 pounds was delivered

CASE 5 A primipara, at term, with cervix three fingers dilated Before onset of labor patient was convalescing from an attack of influenza Indications for operation were simple pelvis, unengaged frank breech after 18 hours of ruptured membranes and 24 hours of active labor disproportion between a large baby and a normal pelvis Temperature at time of operation was 100 8 The puerperium was complicated by repeated pulmonary embolic attack (three) manifesting itself by sudden onset of pain in chest, shock, and bloody sputum Temperature returned to normal on the fourteenth day and patient was discharged improved on the sixteenth day, at her request, to finish convalescence from chest condition at home Abdominal wound healed by primary intention Living baby weighing 8 pounds ounces was delivered

CASE 6 A secundipara, at term, with membranes intact, cervix two fingers dilated Previous pregnancy terminated in spontaneous delivery of a 7 pound 7 ounce baby Indications for operation were flat pelvis, unengaged head after 26 hours' labor fetal distress as evidenced by irregularity of fetal heart sounds, varying from 120–200 in an 8 lb large baby Temperature of mother at time of operation 101 6 degrees Puerperium was uneventful, healing taking place by primary union Temperature returned to normal on the fourth day and patient was discharged cured on the thirteenth day postpartum A living baby weighing 8 pounds 2 ounces was delivered

CASE 7 A primipara, at term, with cervix four fingers dilated, brow presentation Indications for operation were simple pelvis with cephalopelvic disproportion, and presentation unengaged after 20 hours of ruptured membranes and 30 hours of active labor Temperature at time of operation was 101 6 degrees Pre-operative catheterization was productive of a bloody urine Bladder tested at operation was found to be intact Evidence of vesicovaginal fistula appeared on the sixth day after operation Temperature returned to normal on the eighth day and patient was discharged on the tenth day after signs of fistula had disappeared, to reappear again on the third day of her home stay A permanent indwelling catheter for the next 10 days served to bring about a complete cure of her bladder injury A living baby weighing 9 pounds 1 ounces was delivered

CASE 8 A primipara, at term, with cervix two fingers dilated Indications for operation were a 36 year old primipara, 9 year sterility baby important, funnel pelvis, unengaged head after 24 hours of ruptured membranes and 27 hours of active labor Three vaginal examinations were done in hospital Temperature at time of operation was 101 2 degrees Puerperium was uneventful, the wound healing by primary union Temperature returned to normal on the ninth day and patient was discharged cured on the eleventh day A living child weighing 7 pounds 4 ounces was delivered

CASE 9 A quadripara, at term, with membranes ruptured for 8 hours, in active labor for 30 hours, head unengaged The family physician had attempted a high forceps operation in the patient's home with cervix incompletely dilated The forceps slipped, the cervix was lacerated and patient went into shock She was removed to the hospital, treated for shock, and then removed to the operating room Indications for operation were simple pelvis, cephalopelvic disproportion, previous attempt at high forceps, lacerated cervix impending rupture of the uterus. Temperature at time of operation was 101 8 degrees. Puerperium was uneventful, healing was by primary union. A stillbirth infant weighing 10 pounds 3 ounces was delivered Temperature returned to normal on the eighth day and patient was discharged cured on the eleventh day

CASE 10 A primipara, at term, with cervix three fingers dilated, head unengaged, suspected mentoposterior presentation Three vaginal examinations were done in the hospital Temperature at time of operation was 100 4 degrees Indications for operation were simple pelvis with cephalopelvic disproportion, malpresentation after 36 hours labor and ruptured membranes for 20 hours The peritoneal cavity was opened, and promptly sutured Puerperium was uneventful, and healing was by primary union Temperature returned to normal on the fourteenth day and patient was discharged cured on the sixteenth day A living baby weighing 8 pounds 1 ounces was delivered

CASE 11 A primipara, at term, with cervix three fingers dilated Two vaginal examinations were done in the patient's home Indications for operation were funnel pelvis, head unengaged after 36 hours of labor membranes ruptured for 11 hours, per echinipara Patient's temperature at time of operation was 100 4 degrees Bladder was lacerated at operation, and promptly sutured Temperature returned to normal on the twelfth day, and patient was discharged cured on the fifteenth day With the aid of a permanent indwelling catheter bladder was healed by the tenth day A living baby weighing 8 pounds 9 ounces was delivered

CASE 12 A primipara, at term, 37 years of age Indications for operation were a funnel pelvis, non-engagement after 30 hours of ruptured membranes, and 4 hours of active labor Temperature at time of operation was 100 4 degrees Three rectal examinations had been made but none per vaginam. Puerperium was uneventful Temperature returned to normal on the tenth day healing was by primary intention, and patient was discharged cured on the fourteenth day A living baby weighing 7 pounds 4 ounces was delivered

CASE 13 A primipara, at term Indications for operation were a funnel pelvis, an unengaged frank breech after 36 hours of ruptured membranes and 36 hours of active labor Six vaginal examinations were done in the hospital Temperature at time of operation was 101 6 degrees Puerperium was complicated by suppuration of the abdominal wound Temperature returned to normal on the tenth day postpartum, and patient was discharged cured on the fourteenth day A living baby weighing 7 pounds 8 ounces was delivered

CASE 14 A primipara, at term, with cervix four fingers dilated Indications for operation were a funnel pelvis, non engagement after hours of active labor and membranes ruptured for 7 hours Patient had four vaginal examinations Temperature at time of operation was 103 0 degrees Puerperium was complicated by pulmonary embolus and infarct of the spleen Temperature returned to normal on the thirty sixth day and patient was discharged cured on the forty second day A living baby weighing 8 pounds was delivered

CASE 15 A primipara, at term, with cervix four fingers dilated Indications for operation were a funnel pelvis, non engagement after 48 hours of active labor and ruptured membranes for 48 hours Temperature at time of operation was 100 degrees Four vaginal examinations were made The peritoneum and bladder were opened at time of operation The bladder was completely healed

TABLE I—SUMMARY OF THE CASES*

Case No.	Indications for operation						Weight	Condition	Day temp. normal	P.O. day of discharge
	Pelvis	Height in in.	Weight of fetus in pounds	Dilatation of cervix (fingers)	Temperature	Complications of labor				
1 I	Flat		45	2	[illegible]	Fecal retention	6-12	Living	21	25
2 I	Flat	2	5	Full	[illegible]	Tissue values [illegible]		Grandi[illegible]	9	22
3 I	Flat	[illegible]	[illegible]	II	[illegible]	Preeclampsia	9	Living	13	16
4 I	Flat	[illegible]	13	IV	[illegible]		[illegible]	Living	18	15
5 I	Normal	1	5	III	[illegible]	Fecal [illegible]	[illegible]	Living	14	17
6 II	Flat	2		II	[illegible]	Fecal [illegible]	[illegible]	Living	1	11
7 I	Normal	1	[illegible]	IV	[illegible]	Breech presentation [illegible]	[illegible]	Living	8	12
8 I	Flat	2	1	II	[illegible]	[illegible]	[illegible]	Living	9	11
9 IV	[illegible]		5	[illegible]	[illegible]	Hemorrhage [illegible] Vaginal laceration [illegible]	10	Stillborn		11
10 I	Normal		10	III	[illegible]	Impacted [illegible]	[illegible]	Living	11	10
11 I	Flat	3	11	III	[illegible]	Preeclampsia	[illegible]	Living	1	15
12 I	Flat	2	[illegible]	[illegible]	[illegible]		[illegible]	Living	10	14
13 I	Flat	1		[illegible]	[illegible]		[illegible]	Living	10	14
14 I	Flat			IV	133		[illegible]	Living	17	4
15 I	Flat	4	4	IV	102		9	Living	10	14
16 I	Flat	4	[illegible]	IV	Not recorded	Attempt at high forceps on incompletely dilated cervix in horizontal. Laceration of cervix. Shock	8	Living	13	14
17 I	Flat	[illegible]	[illegible]	Full	[illegible]		[illegible]	Living	10	12
18 I	Flat	1	1	Full	100	Frank breech	[illegible]	Living	11	11
19 I	Flat (from contr.)	11	11	III		Manual dilatation	[illegible]	Living	6	14

*All cases were at term.
All presenting parts unengaged at time of operation.

by tenth day at which time temperature returned to normal. Patient was discharged cured on the fourteenth day. A living baby weighing 9 pounds was born.

CASE 16. A primipara, at term, with cervix four fingers dilated. Numerous vaginal examinations had been made. Indications for operation were a flat pelvis, non engagement after 24 hours of active labor, and 24 hours of ruptured membranes. The family physician attempted a high forceps operation on an incompletely dilated cervix. The cervix was lacerated, patient in shock. Patient had fallen bodily from delivery table to floor when she was left unattended and was coming out of the anesthesia and shock prior to operation. Puerperium was uneventful, temperature returned to normal on the twelfth day postpartum, and patient was discharged on the fourteenth day. Healing took place by primary union. A living baby weighing 8 pounds was born.

CASE 17. A primipara, at term, with cervix completely dilated. Indications for operation were non engagement after 60 hours of active labor, membranes ruptured for 60 hours, flat pelvis. Numerous vaginal examinations had been made. Temperature at time of operation was 102.0 degrees. Puerperium was uneventful, healing took place by primary union. Temperature returned to normal on

TABLE II —OPERATIVE COMPLICATIONS

Case	Nature of complication	Treatment	Result
	Peritoneum opened	Immediate suture	
10	Peritoneum opened	Immediate suture	
	Laceration of bladder	Repair with indwelling catheter	Healed in weeks
1	Peritoneum and bladder opened	Immediate suture	Healed on discharge
19	Peritoneum opened Bleeding from broad ligament	Suture of peritoneum	

the tenth day and patient was discharged cured on the twelfth day A living baby weighing 7 pounds 8 ounces was delivered

CASE 18 A primipara, at term, with cervix completely dilated Indications for operation were flat pelvis, non-engagement of a frank breech, in labor for 24 hours, membranes ruptured for 18 hours Temperature at time of operation was 100 0 degrees Two vaginal examinations were done in the hospital The puerperium was complicated by a utero-abdominal fistula, which closed on the tenth day Temperature returned to normal on the thirteenth day, and patient was discharged on the fourteenth day A living baby weighing 6 pounds 3 ounces was born.

CASE 9 A primipara, at term, with cervix three fingers dilated After the patient had been in labor for 40 hours, *the family physician decided that dystocia was due to a* rigid cervix He thereupon proceeded to do a manual dilatation, but was unsuccessful in his attempt Indications for operation were generally contracted flat pelvis, non engagement after 44 hours of labor and a like duration of ruptured membranes, previous attempt at *accouchement a force* The peritoneum was torn because the operator strayed too far afield, thus getting into the thin posterior layer of the broad ligament In attempting to sew this rent in the peritoneum, the needle was plunged through *one of the large sutures, and as a result the operative field* was soon obliterated by the bleeding Hot packs served admirably to control this, and by the time the operation was completed, the bleeding was completely controlled The patient had a chill and temperature of 101 6 degrees on the first day The cause of this could not be determined Temperature returned to normal on the sixth day and the patient was discharged on the fourteenth day A living baby weighing 7 pounds was delivered

Of the 19 cases described, 12 were operated upon at the Bronx Hospital, and the remaining 7 in hospitals outside Three of the 12 patients were brought to the hospital after prolonged labors at home.

There were 17 primiparæ, 1 secundipara, and 1 quadripara The secundipara had a flat pelvis, though she had delivered a 7 pound 7 ounce baby spontaneously on a previous occasion After 36 hours of active labor the cervix was only two fingers dilated, the membranes intact, temperature 101 6 degrees, while the fetal heart was irregular varying in rate from 120–200, and the baby was large. Cesarean section was considered

TABLE III —POSTOPERATIVE COMPLICATIONS

Case	Nature of complication	Contributing factors	Treatment	Result
	Edema of vulva. Foul lochia	Left broad ligament abscess	Immersion	Healed
	Vesicovaginal fistula	Unsuccessful Cesarean section	Refused operation	Still present
3	Purulent discharge from wound. Foul lochia			Healed by secondary union
	Pyelitis	History of chronic pyelitis	Fluids and alkali mixtures	Cured on discharge
8	Repeated pulmonary emboli	Influenza	Medical	Cured on discharge
7	Utero-vesical fistula		Indwelling catheter	Healed in weeks
11	Suppuration of abdominal wound			Healed by secondary union
4	Pulmonary embolus Infarct of spleen		Medical	Cured
18	Utero-abdominal fistula	Slough of suture wound		Healed
19	Chill with temperature of 101 first day after operation			Cured

the logical method of delivery in the interests of the baby and the Latzko technique preferable in the interests of the mother An 8 pound 2 ounce baby living, and an uneventful recovery of the mother was the result The quadripara had an ample pelvis Her labor was conducted at home by her family physician At the end of 30 hours of labor during the last 8 of which her membranes were ruptured, the physician attempted a high forceps with the cervix only four fingers dilated The forceps slipped, the cervix was lacerated, and the patient went into shock This was an evident case of cephalopelvic disproportion between an ample pelvis and a huge baby (10 pounds 5 ounces) obstetrically mishandled The patient was removed to the hospital where she was treated for shock Fear that any attempt at delivery from below with an already lacerated cervix would eventuate in a ruptured uterus, prompted the choice of cesarean section (Latzko) in the interests of the mother a dead baby 12 *sitrs* notwithstanding. She made an uneventful recovery

All pregnancies in this group of cases were at term.

The pelvis was normal in 4 cases, flat in 8 cases, generally *contracted flat in 1 case*, and funnel in 6 cases The indications in the normal pelvis group were as follows fetopelvic dispro-

TABLE IV —LATZKO OPERATION IN CASES WITH NORMAL PELVIS

Case	Indications for operation			Baby	
	Hours in labor	Hours with ruptured membranes	Complication of labor	Condition	Weight lbs
5	24	18	Frank breech—floating Feto-pelvic disproportion In fluenza	Living	8–12
7	30	20	Brow presentation Cephalo-pelvic disproportion	Living	9–11
9	30	8	High forceps attempt at home on an incompletely dilated cervix Shock Cephalo-pelvic disproportion	Still birth	10–5
10	26	10	Impacted mento-posterior Cephalo-pelvic disproportion	Living	8–12

portion with frank breech (baby 8 pounds 12 ounces), primipara, cephalopelvic disproportion, brow presentation (baby 9 pounds 11 ounces), primipara, cephalopelvic disproportion, vertex presentation, previous attempt at high forceps with laceration of cervix (baby 10 pounds 5 ounces) quadripara, cephalopelvic disproportion, impacted mentoposterior (baby 8 pounds 12 ounces) primipara (Table IV)

Active labor lasted as little as 4 hours (primipara with funnel pelvis whose membranes had been ruptured for 52 hours without any attempt at engagement), and as high as 72 hours (primipara with funnel pelvis, membranes ruptured for 72 hours, no engagement) The average duration of labor was 32 6 hours

The membranes were unruptured in only 1 case (secundipara with flat pelvis, previous spontaneous delivery, cephalopelvic disproportion, failing fetal heart, slowly dilating cervix, two finger dilatation after 26 hours of active labor, large baby (8 pounds 2 ounces), mother's temperature 102 6 degrees) At the other extreme, the membranes were ruptured for 72 hours, with a like number of hours in labor, funnel pelvis The average duration of ruptured membranes was 30 3 hours

Engagement of the presenting part had not taken place at time of operation in all cases in this group The presentations were vertex, 14, brow, 1, face, mentoposterior, 1, and frank breech, 3

Vaginal examinations will not be summarized because of the unreliability of figures given by family physician while patient was at home or in hospital Some patients had had no vaginal examinations, rectal examinations having been employed to determine the cervical dilatation, while others had had as high as 6 vaginal examinations

TABLE V —INFANT MORTALITY

Case	Indications for operation	Weight of baby lbs	Autopsy
2	Unsuccessful craniotomy Impending rupture of uterus 46 hour labor with 8 hours ruptured membranes	6+	
9	Attempt at high forceps at home on an undilated cervix Cervical laceration Shock Cephalo-pelvic disproportion	10–5	Cerebral hemorrhage

The smallest baby was 6 pounds (craniotomized), and the largest 10 pounds 5 ounces The average weight was 8 pounds Of the 19 babies there were only two stillbirths (10 5 per cent). One was a craniotomized baby, the other resulted from a high forceps attempt in the patient's home, and was already dead when patient was brought to the hospital Autopsy on this baby revealed a cerebral hemorrhage as the cause of death Among the 17 live births was one whose delivery by high forceps had been attempted by the family physician prior to operation There were no neonatal deaths (Table V)

The peritoneum was opened in 4 cases Immediate suture prior to incising the uterus prevented an initial spill In Case 1 patient developed an exudate in the left broad ligament with an edema of the vulva as a result of lymphatic block, purulent lochia, and temperature for 21 days She was discharged cured on the twenty-fifth day Case 10 made an uneventful recovery In Case 15 both peritoneum and bladder were opened, the latter completely healing by the tenth day The puerperium was otherwise uneventful In Case 19 patient had a single chill with temperature of 102 6 degrees on first postoperative day Puerperium otherwise uneventful (Table II)

There were four bladder injuries One of these (Case 2) was not directly attributable to the Latzko procedure *per se* The operation was done on this patient following a 46 hour labor, unsuccessful attempt at craniotomy which was halted with the development of a contraction ring and rupture of the uterus seemed imminent Catheterization before operation was productive of a bloody urine, showing that trauma to the bladder had already occurred as a result of two factors (1) a prolonged labor where the bladder was suffering a continued devitalization from the incessant pounding of a hard fetal head on the one hand and a hard resistant pelvis on the other, (2) possible added trauma from the attempts at craniotomy The first factor seems the major

and more probable one for two reasons (1) the bladder wall was intact at completion of operation as was evidenced by the absence of leakage when bladder was refilled before closure of the abdominal wall (2) the appearance of the vesicovaginal fistula for the first time on the sixth day a condition sometimes recorded following spontaneous delivery This was the only permanent injury patient refusing operation for fistula at a later date. The 3 other bladder injuries are attributed to indiscretions in technique. Case 7 was a brow presentation and operation was completed *without emptying* the bladder because the catheter had slipped out and no effort was made to replace it She developed a uterovesical fistula No doubt in this case the bladder wall was caught in the uterine suture line and ultimately sloughed into the uterine cavity The use of retention catheter served to bring about spontaneous healing In Case 11 the bladder was opened with the blunt finger, the injury being attributed to an overdistended bladder In Case 15 both bladder and peritoneum were opened the bladder injury here also explained on the basis of overdistention. The authors lay special emphasis to care in avoiding an overfilled bladder In spite of the fact that dissection was very carefully done with the blunt finger overdistention of an already devitalized bladder wall made it more susceptible to injury Both these cases healed spontaneously with the aid of an indwelling catheter (Table III)

In 18 of the 19 cases the temperature at beginning of operation ranged from as low as 100 to as high as 103 degrees In 1 case the temperature before operation was not recorded Temperature lasted for as little as 4 days to as long as 36 days before returning to normal. The average duration of temperature was 12 37 days

The hospital stay was as low as 10 days to as high as 42 days The average hospital stay was 16 3 days When one considers that every one of these cases ran a temperature before operation, and some had prior vaginal manipulation in one form or another from attempts at forcible dilatation of the cervix to attempts at high forceps, one such patient falling off a delivery room table, the low average duration of temperature of 12 37 days, and the low average hospital stay of 16 3 days are quite gratifying

There were no maternal deaths. Only 4 cases presented serious postpartum conditions. In Case 1 the peritoneum was opened at operation, and patient developed an exudate in the broad ligament with a secondary lymphatic obstruction resulting in edema of the vulva She completely recovered after a 25 day hospital stay Case 3 was the only one left with a permanent injury—a vesicovaginal fistula, which, as has already been pointed out, was due to a devitalization of the vesicovaginal septum with resulting sloughing following a prolonged labor in addition to an unsuccessful *attempt at craniotomy* She refused operation for this condition and left the hospital with normal temperature after a 22 day stay In Case 5, while convalescing from an attack of influenza patient went into labor with an unengaged frank breech She ran a temperature for 14 days, puerperium being complicated by three attacks of pulmonary embolus. She was discharged on the sixteenth day In Case 14 the patient, whose temperature was 103 0 at time of operation, had repeated attacks of pulmonary emboli with an infarct of the spleen. After a 42 day hospital stay she was discharged cured.

A most remarkable feature of the Latzko procedure is the little hemorrhage and shock with which it is accompanied There were no cases of excessive bleeding in this group and no cases of postoperative shock. This, in spite of the fact that most of these cases started off with a temperature at time of operation, and a good many were in poor condition at the time as a result of either prolonged dehydrating and wearing labors, or previous manipulations and attempts at delivery from below It was not uncommon to find a patient, immediately after operation, in better condition than she had been at the start of the procedure. This apparent paradox was accounted for by the following factors (a) patients in shock prior to operation were first treated for the shock with morphine and intravenous glucose any patient, even though not in shock, who had had a prolonged labor with the slightest evidence of dehydration was also given an intravenous infusion of 500 to 1,000 cubic centimeters of 5 to 10 per cent glucose solution (b) the absence of a "peritoneal insult, which is usually occasioned in any of the transperitoneal procedures by an initial spill of an irritating or frankly infected amniotic fluid, and handling of the intestines The operation being limited to the lower *thinned-out*, almost bloodless uterine segment, avoided opening the huge uterine sinuses This coupled with the proper conduct of the third stage aided and abetted by the use of the various oxytocics, served well in the prevention of excessive hemorrhage Hemorrhage may result from laceration of large sinuses in the broad ligament when the operator strays too far afield (Case 19)

We believe the Latzko operation is indicated in all cases which cannot be delivered by the vaginal

route for a good and valid obstetrical reason, common knowledge to all well trained obstetricians in addition to which the patient is running a temperature indicative of a potential infection at time of decision in favor of the abdominal route. While not all temperatures are indicative of a potential infection, it seems to us well worth the effort for one to learn the Latzko procedure and apply it in such cases in order better to insure the chances of recovery for these mothers. It is also indicated in a similar group of cases, who although not running temperature, have been repeatedly examined vaginally, and membranes have been ruptured for a long time.

We do not advise the procedure for every case requiring cesarean section. The operation does entail some technical difficulties which can, we are sure be overcome by any obstetrician with a sound surgical background and training. The two-flap and classical operations still have their place and are not without their virtues, but they do not afford the added protection for the mother against shock and peritonitis that can be had with the Latzko procedure.

This procedure is not a panacea for all frankly infected cases, where a baby cannot be delivered intact through the vagina. Unless there is an imminent rupture of the uterus, or an already lacerated cervix from previous attempts at delivery from below which would eventuate in a rupture of the uterus were any destructive operation on the fetus attempted, the operation of craniotomy is still the method of choice, on the living baby already injured, if need be. Where a living baby can be procured by the abdominal route in such a frankly infected mother, and, for religious or social reasons a living baby is imperative, the mother notwithstanding, then the Latzko operation holds out the greatest hope of all abdominal methods. No doubt patients delivered by the vaginal route have developed peritonitis by lymphatic extension. Burns reports a case of peritonitis despite the utilization of the Latzko procedure. DeLee's dictum is very appropriate: "Laparotrachelotomy for all but those where infection is suspected, then Latzko's operation, Porro, or craniotomy."

Where previous attempts at delivery from below had already been made, the obstetrician must appraise the possibilities of a baby remaining alive after delivery by the Latzko procedure. For, to what purpose can an initial surgical risk be ventured, when in the end the baby so obtained will either eventuate in one irreparably damaged, or in a neonatal death. If the one doing the operation was the one who had made the vaginal attempt, then he is in a position to know approximately how much trauma to the baby he had already caused. Armed with this knowledge, he is in a better position to arrive at a decision, for or against the risk of operation in the interests of the child. Where the vaginal attempt had been made by an unskilled practitioner, and there are no contra indications to craniotomy, and it is evident that the baby had already been severely injured, then the destructive operation should be the one of choice in the interests of the mother.

CONCLUSIONS

The Latzko operation is a valuable adjuvant in the armamentarium of every obstetrician. It should not be used promiscuously, but rather in indicated cases only. Its adoption in such indicated cases holds out a definite promise for the reduction of fetal and maternal mortality and morbidity in the "unclean case" group.

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EDITORIALS

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CANCER OF THE STOMACH

HARDLY a situation exists today which challenges the pride of surgery more than that of carcinoma of the stomach The low percentage of operability when the diagnosis is finally made and the patient is sent for operation the low percentage of cures, and the high mortality rates of operations for its relief are all too convincing *evidences that progress in this field is slow* and that there is an opportunity for improvement

In a paper from this clinic dealing with 195 patients with carcinoma of the stomach the operability was only 22 per cent That this is not unusual is evidenced by the fact that in the discussion of a recent paper on this subject read by me before the annual meeting of the Pennsylvania State Cancer Society a good sized clinic functioning in a rural section where patients do not seek early investigation for gastric discomfort reported their operability as only 5 per cent and another group as 7 per cent. It will always be true that where the operability is low the curability will be low and the mortality high.

There are features about carcinoma of the stomach which will make early diagnoses persistently troublesome and a high percentage of cures difficult to attain. The fact that gastric carcinoma tends to diminish gastric acidity rather than increase it brings about gastric comfort rather than the distress which is associated with high gastric acidity The type of carcinoma peculiar to the stomach and the caliber of the stomach are such that when obstructive symptoms occur similar to those warning symptoms present in distal colon cancer the lesion is frequently so far advanced that it is inoperable Similarly gross hemorrhage is so rare in carcinoma of the stomach that as a symptom it has almost no warning value. Persistent occult blood in the stools, on the contrary is a quite consistent feature of carcinoma of the stomach and a diagnostic measure all too infrequently used in patients under suspicion for this lesion.

Add to these features the fact that the *stomach has such a rich supply of lymphatics*, that it is constantly subjected to powerful peristaltic waves well calculated to disseminate malignant cells that it has an extremely rich blood supply and that it is partly hidden under the costal margins, making palpation of early lesions here difficult and it at once becomes obvious that to make earlier diagnoses of cancer of the stomach is going to require earlier and more frequent X ray examinations upon relatively intangible evidences and suspicions *of the presence of this disease*

One not infrequently hears and reads that the way to improve our results in cancer of

the stomach is to submit all gastric lesions to radical surgery, in order that a carcinoma may not be overlooked and in order that malignant degeneration of the gastric ulcer does not occur This is, I believe, a wrong attitude, and, were it employed on a large scale, the operative mortality would at least approximate, if not surpass, the percentage of gastric carcinomas which are missed under the plan of pre-operative segregation by frequent X-ray observation while under a short period of hospital observation under medical management What one has to decide in gastric lesions is, are we dealing with an ulcer which has degenerated into malignancy or with a malignancy which has ulcerated?

More and more gastro-enterologists and surgeons are coming to believe that the percentage of malignant degeneration (if such a condition really exists or the lesion is a malignancy from the start which has ulcerated) is quite low, 5, 6, or 7 per cent The entire question of the percentage of malignant degeneration of gastric ulcer is open to great possible error, not only in the pre-operative decision but also as to the microscopic diagnosis of malignancy

What one's attitude should be toward all gastric lesions is that they must all be suspected of malignancy and that unless these patients can be made symptom free by non-operative measures, and all X-ray evidences of the gastric lesion made to disappear completely, then they must fall into the group of probable carcinomas of the stomach, and radical surgery and its attendant risks accepted as justifiable

What is obviously most needed in carcinoma of the stomach is earlier diagnosis To accomplish this, the physician must submit his patient, particularly when he is more than 30 years of age, to bismuth X-ray and fluoroscopic examination of the stomach, whenever digestive symptoms persist beyond a week's time Patients of this age or past must not treat digestive disturbances lasting over a week by means of the various advertised indigestion remedies, they must seek advice with the definite idea in mind that, if indigestion has persisted for more than a week or repeatedly recurs, they should be examined to determine if the lesion is malignant

As I have said before many times in discussing this subject if we are to discover gastric cancer earlier, doctor and patient alike, must understand that in a great majority of cases the X-ray examination for gastric cancer will be negative so that rather than be critical of the expense to which he has been put for X-ray examination, the patient should be thankful that his doctor has taken such precaution, doubly so when the findings are negative but even more appreciative when the doctor's wise forehandedness has made early diagnosis possible and he is thus offered a chance of being cured

Because so many patients with cancer of the stomach come for operation late, the end-results as relates to cures are poor, and the general attitude on the part of the surgeon and physician toward this lesion is depressingly pessimistic One has but to look back a few years on carcinoma of the rectum to recall how pessimistic and depressing was the attitude of patient and doctor, how low the operability, and how high the operative mortality This has now been gratifyingly changed Of our patients with cancer of the rectum who have had the radical operative procedure, 46 per cent are alive and well over 5 years The operative mortality has fluctuated with operability from 8 to 12 per cent and the operability has increased in the last 2 years from 54 to 70 per cent

From the point of view of operability, operative mortality or curability, cancer of

the stomach, for the reasons given herein will never be as satisfactory a lesion to treat as cancer of the rectum results can be greatly improved however In fact, much of the improvement has already been made

Many surgeons in this country have acquired experience and skill with the operation of partial gastrectomy and with the recent advances which have been made in the production and maintenance of anesthesia a surgeon can do this operation with greater ease for himself and with greater safety for the patient. *Improved diagnostic measures* are also available for early diagnosis. One pressing need remains, however to secure improved results in this field and that is the opportunity to make earlier diagnoses so that the advances in gastric surgery may be applied in the early stages of the lesion when better chances of cure can be offered All the groundwork for improvement in this field has been accomplished except the education of the public to refrain from self treatment of indigestion and to submit to early and complete investigation in the presence of gastric distress and discomfort. FRANK H LAHEY

THE EVOLUTION OF OUR KNOWLEDGE OF THE THYROID GLAND

HISTORICAL contemplation of medical progress is a fascinating pastime —particularly so when it deals with the physiology and pathology of so extraordinary an organ as the thyroid gland

In 1806 in a communication entitled, An Inquiry into the Functions of the Spleen Liver and Thyroid Gland" Benjamin Rush remarked with reference to the greater size of the thyroid in women "that provision is necessary to guard the female system from the influence of the more numerous causes of irritation and vexation of mind, to which they are exposed, than is the case with the male

Observations made in 1879 by Gull, of London marked the beginning of our accurate understanding of the physiology of the thyroid gland. In that year he described a condition to which he applied the term "cretinoid"—one characterized by dryness of the skin, flabby features, swelling of the hands, and retardation of the mental processes

In 1883 Theodore Kocher reported results following the removal of the thyroid in a series *of 101 patients the mortality being 11 8* per cent. He discovered subsequently that with 24 patients on whom he had performed *total* thyroidectomy the final results were uniformly unfavorable These patients rapidly developed symptoms similar to those presented by the myxedematous patients described earlier by Gull. Kocher described the condition by the term "cachexia strumipriva

Experimental work performed by Schiff a year later revealed that total thyroidectomy performed on dogs not only proved fatal but that prior to death tetany became a conspicuous feature The credit for first suggesting that loss of thyroid function is the common cause of cretinism myxedema, and cachexia strumipriva belongs to Sir Felix Semon of *London and by 1880 over 270* papers on the subject had appeared.

In 1891 Murray prepared a glycerol extract from sheep thyroid which he administered subcutaneously to a woman with myxedema a dramatic change occurred in the patient's condition *In 1882* Hadden had noticed that *in myxedema there* was a diminution in the excretion of urea, leading Magnus-Levy of Strassburg in 1895 to suggest that alterations in urea output clearly pointed to altered metabolism as a result he was prompted to investigate the effects of thyroid extirpation on gas exchange and respiratory metabolism, thus

laying the foundation of a knowledge of the chief function of the thyroid gland Magnus Levy noticed that in Graves' disease there was a striking increase in oxygen consumption —the first laboratory demonstration that exophthalmic goiter involved abnormal activity of the gland and that the essential function of the organ was to regulate bodily metabolism and to maintain it at an optimum level

In the same year in an attempt to produce a highly concentrated preparation from the thyroid with more potent physiological activities, Baumann established a fact long suspected that the gland normally contained a high percentage of iodine

In 1886 Mobius of Leipzig suggested that a pathological alteration in the thyroid gland was the primary factor in the causation of Graves' disease Mobius and later Plummer advanced the theory that the syndrome presented by the patient with exophthalmic goiter was due not only to oversecretion but to abnormal secretion as well

Oswald of Zurich, in 1899 studied the protein constituents of the thyroid finding that goiters in which the increased size was due to cellular hyperplasia and in which the colloid was reduced—as occurs in Graves disease—were iodine free, while in colloid goiter great quantities of iodine were present

Coindet was the first to use iodine in the treatment of goiter, although the cures following the administration of burned sea sponges had for over 500 years depended on this element

Pliny was aware of the occurrence of goiter in pigs Writing in 1271 Marco Polo says of the people of one of the countries he visited "They are in general afflicted with tumors in the throat occasioned by the nature of the water which they drink " While painting the roof of the Sistine Chapel Michelangelo penned a sonnet to a friend which begins with these words

> I've grown a goitre by dwelling in this den
> As cats from stagnant streams in Lombardy
> Or in what other land they hap to be

As early as 1703 treatises devoted entirely to the subject of goiter and cretinism began to appear the first from the pen of Gauthier

In 1830 Prevost, of Geneva, argued that goiter was an iodine deficiency disease and that the fault was in the water supply, while about the same time Boussing Ault was led by his work in the Andes to recommend the official sale of iodine as a prophylactic measure In 1852 Chretin suggested that the water supplies in goiterous districts should be enriched with iodine

In 1907 Marine demonstrated that 90 per cent of the dogs in the city of Cleveland showed some degree of enlargement He also showed that as soon as the glandular iodine fell below normal, hyperplasia became detectable and that the amounts of stainable colloid varied inversely with the hyperplasia and directly with the iodine content

In 1919 Kendall of the Mayo Clinic succeeded in obtaining a crystalline substance containing 65 per cent of iodine which exhibited the physiological effects associated with the thyroid gland and to which he applied the name "thyroxin "

In 1926 the problem was taken up by Harrington, of the University of London, whose mode of attack began with hydrolysis of the gland tissue with dilute barium hydroxide In 1927 thyroxin was synthesized by Harrington and Barger

The influence of the thyroid on growth is striking In 1914 Gudernatsch utilizing tadpoles demonstrated the remarkable effect of the gland on this process

The direct effect of thyroxin on the heart muscle has lately been demonstrated The

recent experiments of Lewis and MacEachern prove that the tachycardia of thyroxin treated rabbits continues for hours even after the heart has been transferred to Ringer's or Locke's solution.

Smith and Allen have recently demonstrated that the anterior lobe of the pituitary is *truly the controlling influence in the functional state* of many organs, particularly the thyroid sex glands, and adrenals. Sufficient work has appeared to prove conclusively that the thyroid may be stimulated by it, and in all likelihood, by this agent only

More recently it has been noted that injections of estrogenic substances induce definite histological changes in the thyroid epithelium In the complex interrelationships existing between the hormones and the endocrine system it has been suggested, notably by Bodansky that thyroxin influences the hypoglycemic action of insulin

Marine and Baumann, who have for years studied the thyroid and suprarenal relationship conclude that the hormone from these glands, acting through the anterior pituitary lobes have definite influences, not only on the thyroid gland, but on all endocrine tissues

We are finally justified in accepting with Marine the conclusion that simple goiter is a manifestation of a work, or compensatory hypertrophy which is primarily produced by the thyrotropic hormone of the anterior pituitary in response to the normal or abnormal demand of the organism for increased thyroxin largely influenced by the need of the body for iodine

These are a few of the thousands of landmarks in our far flung journey of thyroid exploration and discovery

HAROLD L. FOSS.

LANDMARKS IN SURGERY

ABRAHAM COLLES

His Outstanding Contribution to Surgical Anatomy

JAMES K STACK, A.B, M D, Chicago, Illinois
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HISTORY tells us that a comparatively high state of civilization existed in Ireland during the early centuries of the Christian era It is reasonable to infer, therefore, that these ancient Irish were not ignorant of the principles and the practice of medicine In the centuries immediately preceding the nineteenth, however, Ireland was a most unhappy country The population was small, poverty was the rule, and only in Dublin were there offered opportunities for higher education Strife was rampant and there was little indeed to encourage men of ability to study and practice medicine But with the years that usher in our story a new medical era dawned The College of Physicians and the College of Surgeons were both granted charters, and medical teaching at the universities in Dublin was given a needed impetus About the time this movement was getting well under way, Abraham Colles was born His biographers give us July 23, 1773, as the date, and the place, Millmount, Kilkenny, where his family had settled two generations before His grandfather had been a medical man, but his father operated an extensive quarry of the famous Kilkenny marble

The education of young Abraham was the best available in the vicinity of Kilkenny, and, when the time came for him to enter the university, he was well prepared Legend has it that he became interested in the study of medicine through the finding of an old book of anatomy washed on his father's property by the flood waters of the river Nore, which coursed through the Colles estate The owner, a local doctor, on the return of the book, noticed the boy's interest in the subject and encouraged him, with the result that on completion of his basic schooling, in 1790, he decided to go to Dublin for the first part of his university work

Not being a brilliant student, Colles gathered no academic laurels He was, however, an intensely interested student, and his assiduous application won for him an apprenticeship to the resident surgeon in Steevens Hospital, Dublin It was in this position that the traits which were to characterize his later work found the first abundant outlet With plentiful material and no other interest, he developed the power of simple observation and the copious case notes he left at the end of his service are still in existence. It was this observation of apparently insignificant signs that was to lend his name to one of the most common, yet least understood, of surgical lesions It may have been that he was also activated in his work during his apprenticeship by the desire to elevate himself to the resident's post when he completed his schooling That the residency at such a hospital was a choice post is appreciated when we recall to mind that as such he could teach privately and thus add to the meager stipend which the beginner in Dublin could hope to earn

After 5 years at the university in Dublin he chose Edinburgh as the school from which he was to receive his degree in medicine This he obtained after two sessions of work, and was then confronted with the problem of where to practice He wanted to return to Dublin, where he had made friends and where relatives lived, but neither group could offer any special assistance in developing a practice Therefore he decided to go to London where he might visit the schools and hospitals and, perchance, light upon some opportunity This opportunity came, not in lucrative form, but in a way to develop himself in anatomy Sir Astley Cooper, destined to be the leading English surgeon of his time, was then a young man engaged in the study of the anatomy of hernia Colles assisted him in this work and in doing so conceived the idea of later publishing his own *Treatise on Surgical Anatomy* for which work we are particularly indebted He constantly decried the older methods of teaching anatomy, and insisted that it should be the principal fundamental science in the training of a surgeon. The method of teaching anatomy by systems, with no correlation, he deplored, and more so the fact that,

Abraham Colles
1773–1843

Diagram of Colles' fracture

given in the light of an abstract science, it could not and did not give the student or the surgeon the opportunity to apply the little he might know to the work of the operating room In the opening pages of his treatise he devotes considerable space to such a thought, and says, among other things

> The student who has been employed in acquiring an anatomical knowledge of the different divisions or systems of the human body has but encountered all the difficulties, without securing any of the benefits For such a plan of study can neither enable him to form a perfect idea of the structure of any part of the body nor can those partial and detached views of the anatomy in any degree qualify him to perform a surgical operation The study of anatomy has generally ceased at that point where it begins to be useful

In 1797 Colles left London, having accomplished two things—developing the friendship of Cooper and laying the groundwork of a thorough knowledge of anatomy He returned to Dublin and to two years of distinct unhappiness His start was anything but promising, and it was only with the utmost courage that he was able to keep in mind the goal he had set for himself Army life and that of the provinces tempted him, but in 1799 he returned to Steevens Hospital at his own solicitation, this time as resident surgeon, a post which, during his apprentice years, it would have been most natural for him to covet

This appointment marked the turning point in his career and the beginning of his phenomenal ascent to the leadership of surgery in Ireland At Steevens was available abundant material of clinical, operative, and autopsy variety The latter still presented the medical profession with many difficulties, but the authorities were beginning to realize the importance of this field to medical progress, and it was rare that grave robbing and other illegal methods of obtaining postmortem material had to be resorted to Colles rapidly became known as a promising surgeon, not only because of his manual dexterity but because of his diagnostic skill and judgment The private classes in anatomy and surgery which he instituted at the beginning of his residency flourished, and he added to his other qualifications that of a thorough and inspiring teacher His private practice developed slowly but steadily and the records which he kept show that after 3 years his income reached between 400 and 500 pounds This increased rapidly as his position in Dublin advanced, and in the prime years of his career his fees never aggregated less than 5,000 pounds

The next important step in the rise of Colles, after his appointment to the surgical residency at Steevens, was his elevation to the chair of anatomy and surgery at the Royal College of Surgeons in Ireland a post he was to hold jointly with Mr Dease This advancement came shortly after the Royal College obtained his services as a lecturer and it was in such capacity that he was able to instill in his colleagues and students his outstanding zeal, patience, and inquisitiveness The desire for professional education increased markedly and he became the most popular teacher in the city With the increase in the number of students, there followed an increase in the productiveness of the various units of the school and hospital with which he was associated Research departments, of course, were not endowed and organized as we see them now and only a few of those proved concepts which have revolutionized medical thought were known at that time. For this reason the investigative work of Colles and his associates was almost entirely clinical in nature Because of the absence of precise diagnostic procedures, their most effective weapon was the power of observation This Colles practiced, and this he taught during the 32 years of his professorship To see to feel, to judge, and to act to be the first to admit one's mistakes, both to one's self and to one's colleagues These were the fundamental precepts in the teachings of this man Little wonder then, that at one time the Royal College of Surgeons in Ireland counted more pupils than any other similar institution in Great Britain. Figures, too are convincing in this regard, for we find that the number of medical students in Dublin in 1836 was nearly 1,000, while in 1800, when Colles himself became a member of the College, but 60 was the yearly average. This fact may well have been but one expression of the cultural advance Ireland made in this period, but if any one man in Irish medicine personified that advance, that man was Abraham Colles

The paucity of Colles writings is to be regretted. His critics might, with some justification, hold that a man with such opportunities to observe, to operate and to record his successes and failures, is in duty bound to enlighten his less fortunate confreres by writing and speaking They in turn, might apply his conclusions to their own advantage and to the advantage of their patients His work in surgical anatomy never completed the studies he made in the treatment of syphilis his contribution to the surgery of vascular disease, and, most important, his observations on fractures of the radius, are all that remain of his works in printed form The explanation for this probably can be found by a study of his character He was eminently retiring and avoided publicity of any kind In his recorded lectures and papers is found an absence of all eloquence and show He abhorred statements loosely made, without adequate foundation, and in his classes he took every opportunity to repress premature theorizing on the part of his pupils He took the view that medical practice would always have in it an element of speculation, the success of which would depend largely upon the individual Facts, one upon the other made for progress, and these alone should be passed on for future use He was fully aware that the theories of one generation were cast aside by the

facts of another It is quite easy to see how a man whose writings suggest such thoughts would be extremely cautious about what he advocated

In 1807 Colles married the daughter of a Galway rector and took a small house on Stephens Green in Dublin As his family grew he found it necessary to move to a larger home in the same square, which he occupied for the remainder of his life

In the quiet study of this big house, Colles, in 1814, assembled the data he had gathered about a certain injury to the wrist The exact nature of this injury, a common one, was in doubt, and there was no unanimity of opinion about it among the surgeons of that period It was agreed that the lesion was usually the direct result of a fall upon the outstretched hand, the hand being used to lessen the force of the impact on the body The most common belief, however, was that a radiocarpal dislocation had taken place Among the adherents to this theory we have no less a light than Sir Astley Cooper, who said—"I have seen this accident frequently and at first did not understand the real nature of the injury Indeed, dissection alone taught me its real character that there is evident projection of the radius and ulna on the dorsal surface, and of the carpus on the palmar surface of the forearm" Colles was unfortunate in that he had had no opportunity to inspect openly after death the state of the bones about such a wrist His conclusions, which differed sharply from the thought current at the time, were based entirely on the appearance of the wrist and forearm, together with what he could determine by palpation This study "On the Fracture of the Carpal Extremity of the Radius" was published in the *Edinburgh Medical and Surgical Journal*, vol 10, 1814, and has served to make the name of Colles renowned wherever surgery is practiced As Professor R W Smith says in his *Treatise on Fractures in the Vicinity of Joints* "If we except the observations of Petit and Pouteau, there are no earlier accounts of this injury, and the characteristic deformity accompanying it, worth being referred to"

Whether Colles continued his studies of this lesion and corroborated his impressions with subsequent autopsy findings, we do not know We do know, however, that many others did, and a voluminous literature has been developed on this subject The original contribution of this man remains through all the subsequent advances, a landmark in surgery, and a firm block from which others spring in investigations in this field Of course, finer points have been drawn in the morbid changes which take place in this injury, variations in the displacement have been suggested and defined, and other names have been appropriately added to these variations, refinements in treatment have been adopted, and with the advent of the X-ray and the popularization of physical therapy, certainly the convalescence has been shortened But, with all these things, we might in retrospect wonder if our results are correspondingly better than those of Colles, better than those of the man who looked at the patient and not at a film, whose deft fingers gently touched ecchymotic and edematous tissues in a diagnostic maneuver many of us are inclined to neglect, and who, by this combination of remarkably developed powers, was able to say "This simple method of examination enabled me to ascertain that the symptoms actually arose from a fracture" It is true that he placed the site of the fracture a fraction of an inch too high, but who would not agree with Smith, who says, "It must be admitted that he conjectured its anatomical characteristics with tolerable accuracy"

To us, who had no personal contact with him, he remains the outstanding Irish surgeon of his time, and since we must necessarily appreciate him by his own writing and that about him by his contemporaries, this work on the radius remains the bright light of his professional career To his patients, students, and colleagues, however, this work no doubt would pale into insignificance when compared with the man himself It was with the deepest regret that these friends persuaded him to give up his work at the school and the hospital in 1841, because of ill health He did this reluctantly, but kept his private practice as best he could in the two unhappy years that followed Then, sensing the end, he continued to be up and about until his swollen extremities and shortness of breath forced him to bed for the last time

In the few remaining days he might have looked back with pardonable pride upon a most useful and enviable life—that of a beloved father, eminent teacher, skilful surgeon, twice president of the Royal College of Surgeons, and the distinction of having declined a baronetcy because it was offered to honor him as a man, and not as a representative of the medical profession in Ireland Could he have looked ahead he would have seen a public funeral and a vast concourse of friends and representatives from all the kingdom in the procession, he would have noted the cessation of activity in the medical schools of Ireland, and later the preservation of his likeness on canvas and in marble in the halls of the Royal College But the inevitable increase of uremic toxins would have terminated these introspections, for shortly, painlessly, and in a deep sleep, he died.

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CORRESPONDENCE

THE EFFECT OF VIOSTEROL IN JAUNDICE

To the Editor: The paper published by McNealy, Shapiro, and Melnick in the April, 1935, number of SURGERY, GYNECOLOGY AND OBSTETRICS, was presented as a study of the effect of viosterol in jaundice. No particular attention was paid in this study to the general mortality and morbidity statistics at Cook County Hospital, except as it concerned the patients studied. From the nature of the work, we could use only those patients who were in the hospital long enough to have complete bleeding time studies and to receive 1 or 2 weeks of pre-operative preparation. This automatically excluded all patients operated upon as emergencies or after only 1, 2 or 3 days of hospitalization. The patients used, however were unselected as to age, sex, race or general condition also unselected in the sense that the control and definitive patients were taken from the same group.

A subsidiary study of all the gall-bladder and common duct cases operated upon during the period revealed a striking and foreboding difference between the mortality in the group of elective, leisurely and carefully handled cases to which our study was of necessity limited, and the group of desperate emergencies who were hastily operated upon without precise diagnosis and preparation. In our original study hardly any of this latter group was seen by us because they were rushed through before they could be picked up in our rounds or before study and treatment could be gotten under way.

Among 254 elective gall-bladder operations there were only 4 deaths, a mortality of less than 2 per cent. In the emergency group the acute empyemas of the gall bladder showed a mortality of 24 per cent, the acute pancreatitis cases a mortality of 50 per cent, and in the misdiagnoses operated on under the diagnosis of gall-bladder disease and which included cases of coronary thrombosis, empyema, subphrenic abscess, perforative peritonitis from gangrenous appendices and peptic ulcers, etc. the mortality was in the neighborhood of 75 per cent.

In the common duct cases were included not only those patients in whom stones were removed from the common duct at operation, but also those with a history of recurrent jaundice or intermittent hepatic fever and those in whom the common duct was explored even though stones were not found. Here too among 63 elective cautiously and completely studied cases there were 7 deaths, a mortality of 11 per cent. Hasty operating in this group was more rarely indulged in, yet in 6 desperate cases in which operation was done there were 7 deaths, a mortality of 77 per cent. Added together there was an average mortality in this group of 30 per cent.

It is very likely that several of the patients who were operated upon as emergencies would have died without operation. Yet these statistics firmly re-emphasize that in gall-bladder and common duct surgery calm deliberation, careful study and adequate preparation are essential.

McNEALY, SHAPIRO, AND MELNICK
R. B. McNEAL

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE second volume on *Pneumonokonioses (Silicosis) Literature and Laws*[1] up to 1935 is a text, while the first volume, which appeared over a year ago, was more a reference compilation of the history of diseases or afflictions pertaining to silicious or non-silicious dusts Many attempts have been made to define silicosis The definition given by F S Kellogg in an address before the American Bar Association is noteworthy Regardless of the definition of silicosis, most of the proved causes of dust in any form have to be found at autopsy

Those of us who, from association, have been on the firing line during the past several years, with suits amounting to more than $150,000,000 in Illinois, will appreciate what a gift this second book really is E R LeCount has stated in the "Foreword," it is not only opportune, it is overdue The storm of lawsuits reached us and were being tried before this Book II summary was published

We spent nights searching medical literature for something tangible and authentic to assist attorneys trying these cases If Book II had been available, we would not have had so many reference worries The subject index includes abstracts on anthrocosis, asbestosis, cement dust, dust collectors, dust control, dust counts, dust masks, exhaust ventilation devices (including dust fans), the subject of fibrosis, granite cutters disease, gypsum, hematite, occupational disease acts of many States, International Labor conference of 1934, Johannesburg conference, Jones-sericite theory, lung pathology, lung silica content, silica in normal lungs, marble dust, miner's phthisis There are also abstracts on the National Bureau of Casualty and Surety Underwriters conference, pulmonary heart disease, quartz, different types of respirators, roentgenograms' interpretation, sandblasting industry, Saranac Lake laboratory, siderosis, silico-tuberculosis silicosis awards, silicosis diagnoses, silicosis postmortem, silicosis racket, silicosis in urine, tuberculosis relationship, Wisconsin dust code, and many other subjects condensed so that one familiar with these troublesome issues can determine easily if it is necessary to review the original articles for a more elaborate picture of the case in question

The Laws in the United States pertaining to occupational diseases are well abstracted The last word given by each one of the States having laws covering disability payments for occupational disease is given C F Sharkey tells of legislation in the United States, stating that compensation laws are in operation in 44 of the 48 states Only 12 states compensate for occupational disease The Wisconsin Dust Code of allowable dust standards is quoted

> Dust containing less than 35 per cent free silica in a cubic foot of air is allowed to be present in a quantity of 15 million countable particles under 10 microns in longest dimension As the silica percentage increases the number of dust particles allowed to be present decreases Pure silica (SiO_2) is allowed to be present in a quantity of 5 250 000 The first condition for the occurrence of a silicotic process is according to the present investigation that the inhaled dust contains a large percentage of silicon dioxide and that it is possible for this dust to gain an entry into the alveoli provided that is that the particles of dust are not more than 10 microns in size After inhalation the silicious dust chemically or colloidochemically acts on the lung tissues causing them to react resulting in the formation of typical silicotic nodules

Roentgenological findings, necessarily technical, of great value to all, are well presented by Dr H P Sampson, whose experience in dust fibrosis is greater, probably than that of any other X-ray authority in the United States

The discussion of the sericite theory is well given by Professor Haldane and Professor Kettle Much has been written about the mineral, sericite, and the extent of damage it causes to lung tissue

There is one item lacking in the digest of literature for 1934 and that is, reference to non disabling silicosis or any form of dusty lung disease, many employees have silicotic nodules in the lungs but this condition does not constitute disability

In Book II, the authors have brought the subject matter down to the present in an excellent manner One can unhesitatingly endorse the book as outstanding, to be highly recommended for doctors, laboratory workers, claim departments of insurance companies, and lawyers, because it summarizes practically everything that has happened during 1934 in civilized countries throughout the world concerning pneumonokonioses ROY KUHN

IN making a translation of the German edition of *William Conrad Roentgen*[2] Glasser has incorporated minor corrections and revisions Roentgen, a physicist, decided in October of the year 1895 to make some experiments with cathode rays It was during the course of these experiments that, on a Friday evening, November 8, 1895, he made the

[1] THE PNEUMONOKONIOSES (SILICOSIS) LITERATURE AND LAWS OF 1934. INTERNATIONAL ABSTRACTS, EXTRACTS AND REVIEWS OF THE PNEUMONOKONIOSES AND THEIR ASSOCIATED DISEASES AND SUBJECTS By George G Davis M D Ella M Salmonsen and Joseph L Early wine. Chicago Chicago Medical Press (Not Inc) 1935

[2] WILHELM CONRAD ROENTGEN AND THE EARLY HISTORY OF THE ROENTGEN RAYS By Otto Glasser With a Chapter Personal Reminiscences of W C. Roentgen by Margret Boveri Springfield, Illinois, and Baltimore Maryland Charles C. Thomas 1934.

observation which proved to be so significant. After examining and testing all details, he published his observations in a "Preliminary Communication" at the end of December 1895. Few announcements of scientific discoveries have received such rapid and widespread publicity. In a few weeks his communication had been translated into all languages and had become known throughout the world.

The application of the X-ray to medicine was immediately recognized, and the field has grown by leaps and bounds. The author has covered the use of X-ray not only in medicine, but also in non-medical fields.

Interest in the volume is greatly enhanced by the chapter on personal reminiscences by Margret Boveri. The chapter teems with interesting facts concerning Roentgen's youth, education, and character.

The volume should be of interest not only to the radiologist but to all interested in medical and scientific history.

EARL E. BARRY

AS the title indicates, Hoyer's book[1] is a comprehensive review of the anatomy of the lymphatic system as it exists in all the vertebrate groups from the lowest fishes to man. Anyone interested in such details can find in this compilation succinct summarizations and competent bibliographies. At the end is a brief recapitulation of some of the most pertinent comparative facts and an instructive schematic diagram of the lymphatic plan throughout the vertebrate series. To those interested primarily in the medical sciences, the recent volume of Rouvière (1932) will prove more generally useful.

L. B. AREY

[1] MENSCHLICHE ANATOMIE IN VERGLEICHENDER DARSTELLUNG. DAS LYMPHGEFÄSSSYSTEM. DAS WASSERGEFÄSSSYSTEM UND ENTGIFTUNGSORGANE. By Hanzik Hoyer. Leipzig: Leipzigsche de L'Université, 1934.

THE larger part of Safian's profusely illustrated volume[1] of 300 pages is devoted to hypertrophy of the nose and its constituent parts and to saddle nose. Although the author mentions the use of cartilage transplants in the treatment of the latter condition he prefers to use ivory and does not indicate how cartilage transplants can be measured for or adapted to an individual case. He simply states "the transplant is shaped with a sharp scalpel to fit the defect."

Comparatively little space is given to such problems as the broad and asymmetrical nostril with lateral displacement of the ala, deformities of the nose associated with extensive loss of tissue, and complete restoration of the nose. No mention is made of the deformities of the nose associated with retraction of the upper lip and very little space is given to the treatment of recent injuries.

There is abundant pictorial evidence to attest the author's skill in the treatment of hump nose, of hypertrophy of the bony and cartilaginous framework, and of the tip of the nose and the results he has obtained in the treatment of these conditions are admirable. One wishes there were more detailed information for the student who is concerned with the many other problems involved in the surgical treatment of nasal deformities.

SEYMOUR L. KOCH

[1] HYPERTROPHIC NOSE. CHIRURGICAL NEW METHODS. CORRECTIVE RHINOPLASTIC SURGERY. By Joseph Safian, M.D. New York: Paul B. Hoeber, Inc., 1933.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

DOUVERS ANATOMICHES ENCYCLOPÉDIE DE LA CHIRURGIE ET PARAMÉDICALE. By Dr. C. Claisé and I. Bernard. Paris: Librairie Maloine, S.A., 1935.

CHIROPRACTIC OPER. PHILADELPHIA, PA.: CHIROPRACTIC SCIENCE UND ARTISTE. By Dr. Max Sachsenmaier. Berlin: Julius Springer, 1935.

SHORT WAVE THERAPY AND GENERAL ELECTRO-THERAPY. By Heinrich F. Wolf, M.D. New York: Modern Medical Press, 1935.

TRANSACTIONS OF THE FIFTY SIXTH MEETING OF THE AMERICAN SURGICAL ASSOCIATION. Vol. 53. Edited by Walter Estell Lee, M.D. Philadelphia: J. B. Lippincott Co., 1935.

A CENTENARY HISTORY OF THE MANCHESTER MEDICAL SOCIETY WITH BIOGRAPHICAL NOTICES OF ITS FIRST PRESIDENT, SECRETARIES AND HONORARY LIBRARIAN. By Edward Mansfield Brockbank, M.B.E., M.D., F.R.C.P. Manchester: Sherratt & Hughes, 1934.

PRIVY COUNCIL. MEDICAL RESEARCH COUNCIL. THE SOURCE OF INFECTION IN PUERPERAL FEVER DUE TO HAEMOLYTIC STREPTOCOCCI. By Dora C. Colebrook. London: His Majesty's Stationery Office, 1935.

THE PRACTITIONER'S LIBRARY OF MEDICINE AND SURGERY. Vol. 12. NEUROLOGY AND PSYCHIATRY. New York and London: D. Appleton-Century Co., 1936.

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TREATMENT OF PEPTIC ULCER BASED ON PHYSIOLOGICAL PRINCIPLES[1]

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ALTHOUGH considerable progress has been made in gastric surgery in the past two decades, the treatment of chronic peptic ulceration still is not wholly satisfactory. Too frequently the physician's attention is directed to the ulcerative lesion in the stomach or duodenum without his realization that the local lesion is merely a symptom of a generalized disorder. The treatment of the ulcer alone is almost as illogical as the treatment of pyrexia with antipyretics. Unless the underlying factors which are responsible for the predominating symptom in each instance are corrected, the results of therapy are likely to be unsuccessful.

In order to treat a patient with peptic ulceration rationally, it is important to have some conception of its cause. The factors which are responsible for peptic ulceration may be divided into two groups, in one of which are the factors which cannot be controlled, that is, are not amenable to treatment, and in the other of which are the factors which can be influenced by therapy and the correction of which may result in amelioration of symptoms and possibly a cure. The uncontrollable factors which in reality are predisposing ones are (1) *tissue susceptibility* and (2) *constitutional predisposition*. By tissue susceptibility is meant the vulnerability of certain portions of the gastro-intestinal tract to peptic ulceration, namely, the lesser curvature of the stomach (*magenstrasse*), the duodenal cap, the jejunum, and other portions of the intestinal tract subjected to acid gastric secretion, as in Meckel's diverticulum containing islands of gastric mucosa. The predisposing factor, "tissue susceptibility," is present in all individuals but peptic ulcer probably never occurs unless other factors are also operative. "Tissue susceptibility" to peptic ulceration is an inherent quality, which cannot be altered, but the surgeon can refrain from performing operative procedures which will subject abnormally susceptible portions of the intestinal tract to the acid gastric chyme. Matthews and Dragstedt showed that the susceptibility of the intestinal tract to acid gastric chyme increases proportionately with the aboral distance from the pylorus. The susceptibility of the intestinal tract to peptic digestion is illustrated by the occurrence of jejunal ulcers following gastrojejunostomy and the development of peptic ulcers in Meckel's diverticula which contain gastric mucosa. We have been able to corroborate Matthews and Dragstedt's experimental work concerning the susceptibility of the intestinal mucosa to acid gastric secretion. Although trauma by food impingement against the lesser curvature of the stomach has been blamed for the development of ulcers in this area, we believe from

[1]Presented before the Clinical Congress of the American College of Surgeons, San Francisco, October 28–November 1, 1935.

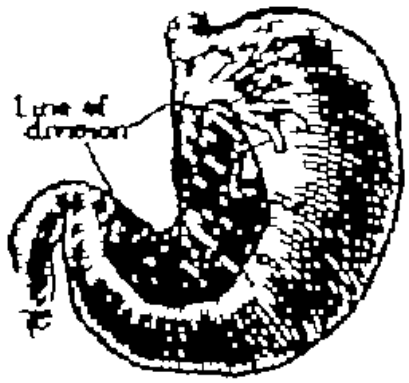

Fig. 1. Diagrammatic drawing showing that portion of the stomach remaining after extirpation of the lesser curvature. No ulcers developed in this group of animals, although in a smaller group of animals in which the greater curvature was extirpated leaving the lesser curvature intact, the incidence of ulceration was 63.8 per cent. (After Ochsner, Gage, and Hoed. Arch. Surg., in press.)

our experimental observations that there is an additional and more important inherent factor which is independent of trauma. In our experiments (33, 67) which consisted of the extirpation of the lesser and greater curvatures of the stomach respectively, the incidence of ulceration in the two groups of experiments varied considerably. In those cases in which the lesser curvature remained after extirpation of the greater curvature, the incidence of ulceration was high (63.6 per cent) (Fig. 1) whereas in those in which the greater curvature remained after the removal of the lesser curvature no ulcers developed. Extirpation of the greater curvature, which in reality is a fundusectomy, as suggested by Connell, resulted in a much higher incidence of ulceration than in animals with the lesser curvature removed, probably because of the greater susceptibility of the lesser curvature to ulceration. Watson found that whereas definite reductions in total and free acidity were obtained immediately after extensive fundic resections in dogs, the decrease was less marked after 4 months. We believe, because of the results of this investigation, that although theoretically and actually fundusectomy results in reduction of gastric acidity, which reduction is not permanent, however, the operation is not justified because the lesser curvature being more susceptible to ulceration is much more vulnerable than is the fundus. These experiments clearly demonstrate the importance of tissue susceptibility.

The "constitutional predisposition" (ulcer diathesis) is probably one of the most important factors as regards the development of peptic ulceration. Although it is difficult to define ulcer diathesis, it hardly can be denied by one with considerable clinical experience with peptic ulcer patients that "constitutional predisposition" does exist. Whether it consists of a peculiar arrangement of the capillaries of the mucosa of the stomach with the production of large submucous plexuses in the subepithelial layers (vasoneurotic diathesis) as demonstrated by Duschl and by Moeller and Heinberger, or of increased irritability of the parasympathetic nerves (vagotonia) as suggested by von Bergmann, or of overactivity of the sympathico-adrenal system, as proposed by Crile, cannot be definitely proved. Draper, Dunn, and Seegal believe that ulcer patients have characteristic anthropometric relations which they designate as "ulcer constitution." The relative importance of "constitutional predisposition" varies in different individuals. Judd and Waldron (40) state that the predisposition to ulceration is especially marked in patients with duodenal ulcer and less so in gastric ulcer patients. Hurst (43) believes that the type of peptic ulcer is dependent upon the habitus of the patient. The patient with a high, short, rapidly emptying stomach (hyperasthenic gastric constitution) with hyperchlorhydria and with little or no mucus in the stomach, usually has duodenal ulcer, whereas the patient with a long, slowly emptying fish hook type of stomach (hypoasthenic gastric constitution) with hypochlorhydria frequently has a gastric ulcer. Morley, in a series of 250 normal individuals, found the stomachs in 7.8 per cent hyperasthenic, in 44.4 per cent sthenic, in 46.8 per cent hypoasthenic, and in one per cent asthenic. In 50 cases with duodenal ulcer the percentages were 5.5, 44.4, and 50.3, respectively. In a correlation between the gastric acidity values and the types of stomach, it was found in this investigation that the acidity was lowest in the asthenic types and highest in the hyperasthenic types. Cushing has emphasized the importance of association of cerebral lesions and peptic ulceration and concludes "it may easily be that highly strung persons, who incline to

the form of nervous instability classified as parasympathetic (vagatonic), through emotion or repressed emotion, incidental to continued worry and anxiety and heavy responsibility, combined with other factors, such as irregular meals and excessive use of tobacco, are particularly prone to have chronic digestive disturbances with hyperacidity often leading to ulcer effects wholly comparable to those acutely produced by irritative lesions experimentally made anywhere in the course of the parasympathetic system from tuberal center to its vagal terminals" The importance of psychic strain as an etiological factor in peptic ulcer is illustrated by Rivers' findings in 200 specialists in medicine Twenty per cent of them had definite peptic ulceration (usually duodenal) and at least an additional 20 per cent admitted taking alkalies at intervals These findings are even more significant when contrasted with the findings in a group of negro patients in none of whom was there any evidence of peptic ulcer Wilkie refers to the individual with "constitutional predisposition" as an "ulcer former," and Yates states that those susceptible to the disease can develop chronic gastroduodenal ulcer Possibly as the result of the constitutional neuromuscular imbalance—vagatonia of Bergmann (10) or sympathico-adrenal hyperirritability of Crile (16)—there frequently occurs spasm or lack of relaxation—achalasia, Hurst (42)—of the pyloric sphincter Whether the condition is a spasm of the pyloric sphincter (pylorospasm) as contended by Ivy (45), Finney (29), Judd and Waldron (49), and Yates (85) or absence of normal relaxation (achalasia) as suggested by Hurst (42), Miller (61), Martin and Burden (56) makes little difference because, in both, gastric retention results

If the above premise is correct concerning the predisposing factors, viz , "ulcer diathesis" and "tissue susceptibility," little can be accomplished as regards the correction of these inherent qualities aside from avoiding those operations which will subject a highly susceptible portion of the intestinal tract to the acid gastric chyme Although as mentioned above "tissue susceptibility" to peptic ulceration is present in all individuals constitutional predisposition occurs comparatively less frequently The concomitant occurrence of these two predisposing factors does not necessarily result in chronic peptic ulceration, however, because unless there are additional exciting or precipitating factors, ulceration probably never occurs The precipitating factors which are controllable, that is, are amenable to therapy, are *hypersecretion and hyperacidity, focal infections*, and *gastric trauma* Hypersecretion and hyperacidity occur normally in many individuals Rehfuss and Hawk found that 40 per cent of normal individuals had gastric hypersecretion, and Bennett and Ryle found persistent hyperchlorhydria in 10 per cent of 100 normal persons The abnormal accumulation of gastric juice may be due to two factors which accentuate each other As the result of pylorospasm or achalasia, there is retention of gastric secretions which, by causing gastric distention, stimulates further secretion (Meek), thus setting up a vicious circle Although hypersecretion may be of little or no significance during the digestive period when food is in the stomach, it is a real danger when present in the fasting stomach as shown by Winkelstein (82) Focal infections are important etiological agents in peptic ulcer as demonstrated by the work of Rosenow and his associates (66) Focal infections may produce specific inflammatory lesions in the stomach wall, as suggested by Rosenow, by Konjetzny, by Orator and Metzler, and by Puhl, or when within the abdomen they reflexly can produce pylorospasm In the former instance the focal infection plays a more or less specific rôle, whereas in the latter its action is entirely nonspecific A factor which may or may not be of importance is trauma to the stomach during digestion Aschoff stressed the danger of trauma to the stomach along the gastric pathway, over which area the gastric mucosa is different from that in other portions of the stomach Mann and Williamson believe that the mechanical impingement of the acid gastric chyme against the lesser curvature of the stomach and the duodenal cap is of etiological importance in the development of peptic ulcer Because ulcers occurred in the jejunum just beyond the gastrojejunal anastomosis in animals with the "duodenal drainage operation," these investigators considered the ulcer-

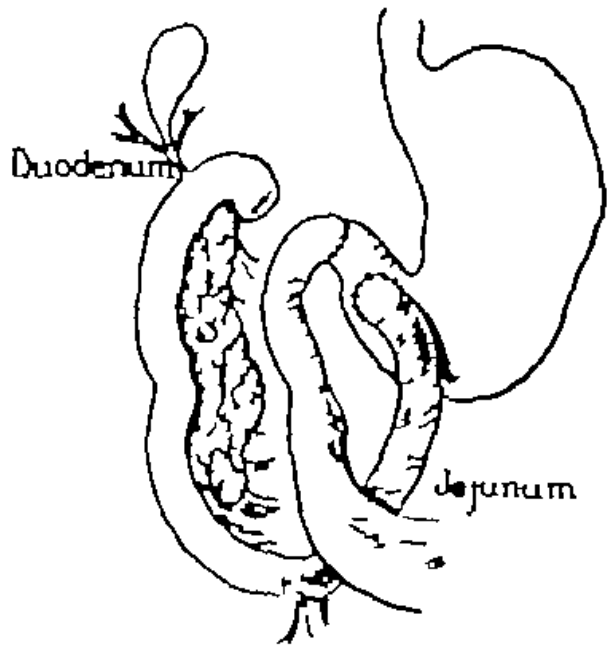

Fig 2. Diagrammatic drawing showing modification of McCann operation with the duodenum anastomosed to the stomach just proximal to the gastrojejunal anastomosis In this way the alkaline duodenal secretions are emptied into the stomach just proximal to the anastomosis No ulcers developed, demonstrating that trauma plays an insignificant role (After Graves Arch Surg 1935, 30 833)

ations the result of mechanical irritation McCann modified the "duodenal drainage operation so that the duodenal secretions were emptied into the stomach instead of into the terminal ileum Because he obtained a high incidence of jejunal ulcerations he contends the mechanical factor is more important than the chemical one Ferguson (27) and Ivy and Fauley (46) found that chronic ulceration of the stomach could be produced experimentally in animals by feeding rough irritating food following excision of gastric mucosa whereas a chronic ulcer would not develop if non-irritating foods were administered. Morton believes that trauma determines the site, whereas chemical factors determine the chronicity of ulcers

It is well appreciated by clinicians and pathologists that superficial erosions of the gastric or duodenal mucosa can occur without producing symptoms and can be of little significance clinically Of interest to the clinician however is the chronic ulcer which persists and does not readily heal as do the superficial erosions which may follow indiscretions in diet or drink Undoubtedly unless a number of the factors mentioned are present, the ulcer will not persist.

As the predisposing factors, "tissue susceptibility" and "ulcer diathesis," cannot be influenced by therapy the treatment of chronic peptic ulcer must consist of the correction of those factors which are controllable viz hypersecretion and hyperacidity focal infection, gastric trauma, and pylorospasm The importance of hypersecretion and hyperacidity is becoming more appreciated by investigators and clinicians. For the past 5 years in the experimental laboratory at Tulane University we have been conducting a series of experiments, the results of which definitely demonstrate the importance of acidity in the production of chronic peptic ulcer Eralto Mann and Williamson (55) and Ivy (44) have been able to produce ulcers by shunting the alkaline duodenal secretions away from the stomach by the duodenal drainage operation The duodenal drainage operation consists of division of the stomach at the pylorus, blind closure of the duodenum, division of the jejunum immediately distal to the ligament of Treitz, anastomosis of the distal portion of the jejunum to the pyloric end of the stomach and anastomosis of the proximal loop of jejunum to the terminal ileum. McCann modified the "duodenal drainage operation" so that the alkaline duodenal secretions were emptied into the fundus of the stomach instead of into the terminal ileum Although McCann contended that mechanical trauma was more important than peptic digestion because of the high incidence of ulcers which he obtained in his experiments, Graves, in our laboratory modifying McCann's technique so that alkaline duodenal secretions were emptied into the stomach just proximal to the gastrojejunal anastomosis (Fig 2) demonstrated that trauma was of little or no significance, because no ulcers occurred in his animals The mechanical arrangement in both Graves and McCann's experiments were identical the only difference being in acidity Presumably because in Graves' animals the alkaline duodenal secretions emptied into the stomach immediately proximal to the gastrojejunal anastomosis, more efficient neutralization of the gastric juice leaving the stomach

was secured than in McCann's experiments To determine the relative protective effects of bile and pancreatic juice in the stomach Graves deviated bile and pancreatic juice respectively into the lower ileum without performing any other operation In the experiments in which the bile was deviated into the lower ileum away from the duodenum only 1 of 8 animals developed an ulcer which healed with the formation of a cicatricial stricture In the group of animals in which the pancreatic juice was deviated away from the duodenum into the terminal ileum no ulcers developed The results in these experiments indicate that normally the duodenum in the dog is resistant to acid gastric chyme even though one of the alkaline secretions is deviated into the terminal ileum There is also a suggestion that bile is possibly slightly more protective than pancreatic juice because one ulcer occurred in the group of animals with only the pancreatic juice and succus entericus to protect the duodenum whereas no ulcers were found in the animals whose duodenums contained bile and succus entericus In other groups of experiments Graves replaced the duodenum by a jejunal loop and attempted to determine the protective influences of bile and pancreatic juice, respectively In one group of animals the common bile duct and in another the pancreatic duct was anastomosed to the jejunum The animals were allowed to recover from these operations but in none did ulcers develop At subsequent operations the duodenum was replaced by a jejunal loop as follows The stomach was divided immediately proximal to the pylorus and the duodenal end closed blindly The jejunum was then divided a few centimeters proximal to the common duct or pancreatic duct transplant The duodenal end was then anastomosed to the terminal ileum, thus deviating the succus entericus and that secretion which had not been deviated into the jejunum by the duct anastomosis The jejunal end was then anastomosed to the pyloric end of the stomach (Fig 3) In this way the duodenum was replaced by jejunum which was protected by only one of the alkaline duodenal secretions In every instance, irrespective of the presence of bile or of pancreatic juice in the jejunum,

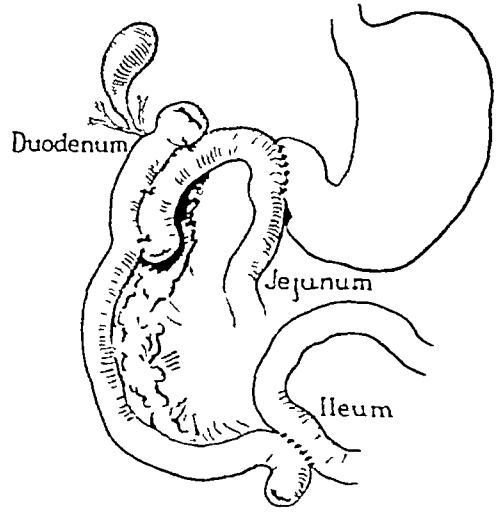

Fig 3 Replacement of duodenum by jejunum. The pylorus has been divided, the duodenal end closed blindly Immediately distal to the ligament of Treitz the jejunum is divided and the duodenal end closed blindly This is subsequently anastomosed to the ileum. The proximal end of the jejunum is closed blindly and anastomosed to the stomach The common bile duct has been anastomosed to the jejunum so that the loop of jejunum is protected only by the bile, the pancreatic juice and the succus entericus being emptied into the terminal ileum (After Graves Arch Surg, 1935, 30 833)

chronic ulcers developed in the jejunum immediately distal to the gastrojejunal anastomosis The results in these experiments demonstrate that the jejunal mucosa is much more susceptible to peptic digestion of the acid gastric chyme than the duodenal or gastric mucosa and that neither bile nor pancreatic juice alone offer sufficient protection against peptic digestion In an extensive investigation we (33 67) demonstrated the rôle of acidity in the production of peptic ulcers By feeding hydrochloric acid and by histamine stimulation over long periods of time, we obtained in 27 per cent of our dogs erosions and superficial gastric lesions but no chronic ulcers In another group of experiments pouches were formed from the lesser and greater gastric curvatures, respectively following which the pouch was anastomosed to a jejunal loop (Fig 4) In the animals with lesser curvature pouches and jejunal anastomoses jejunal ulcers developed in 71 per cent, whereas in those animals with greater curvature pouches and jejunal anastomoses,

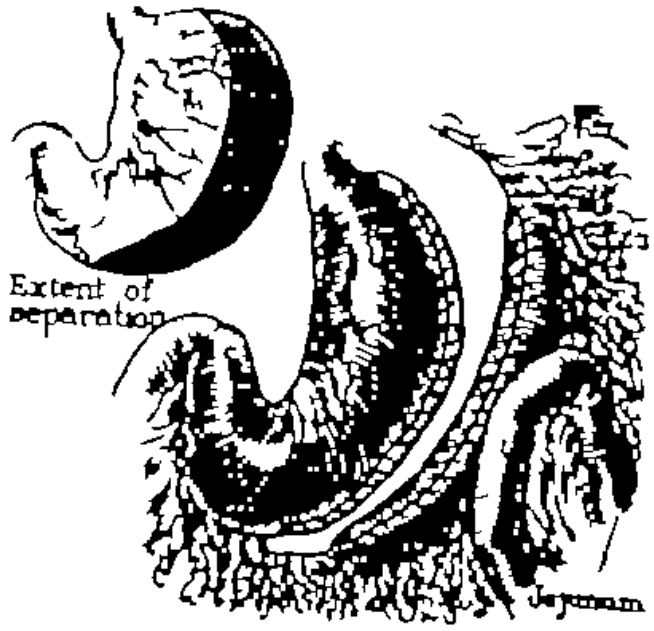

Fig 4 Diagrammatic drawing showing formation of pouch from the greater curvature and anastomosis with the jejunum In 100 per cent of these experiments jejunal ulcers developed, whereas in experiments with a similar pouch formed from the lesser curvature and anastomosed to the jejunum, the incidence of ulceration was 7 per cent (After Ochsner Gage, and Hoxie Arch Surg in press)

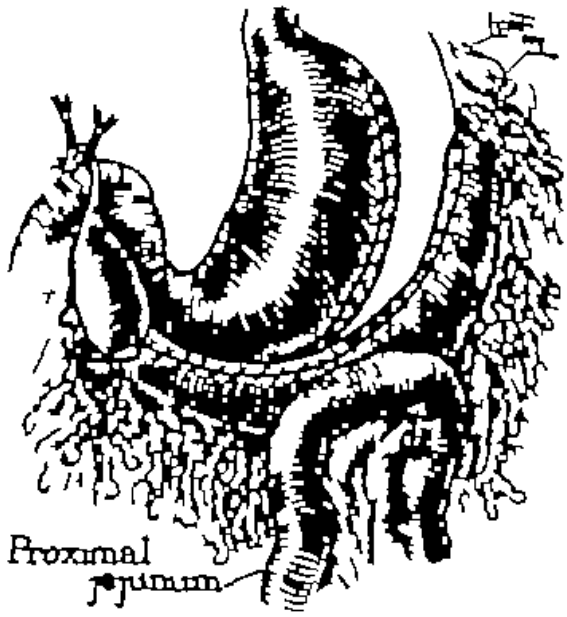

Fig 5 Drawing illustrating formation of the greater curvature pouch with anastomosis to the jejunum and the gallbladder, deviating the alkaline bile into the gastric pouch Following the neutralization of the gastric pouch secretion, the incidence of ulcers dropped from 100 per cent to 28 per cent (After Ochsner Gage, and Hoxie Arch Surg in press)

ulcers of the jejunum developed in 100 per cent. The higher incidence of ulceration in the greater curvature pouch experiments was probably due to the higher acidity in the fundic portion of the stomach which exerted a more marked digestive effect on the susceptible jejunal mucosa. In another group of experiments the greater and lesser curvature pouches and jejunal anastomoses were repeated but in addition the common duct was divided and the gall bladder anastomosed to the gastric pouch, thus deviating the alkaline bile into the respective gastric pouch (Fig 5) The incidence of jejunal ulcers in the lesser curvature experiments dropped to 50 per cent, whereas in the greater curvature pouches it dropped to 28 per cent These experiments *demonstrate the protective value of alkaline* bile in preventing jejunal ulcer

Relatively recently another group of experiments has been performed by DeBakey in our laboratory in which the relative protective values of bile and pancreatic juice respectively were determined As shown by von Haberer (20 per cent) and Chaimont (28 per cent) the pyloric occlusion operation, as suggested by von Eiselsberg in a non-obstructed stomach results in a high incidence of jejunal ulcer DeBakey performed pyloric occlusion operations in normal dogs by dividing the pylorus, closing the duodenal and gastric ends blindly and re-establishing the gastro-intestinal continuity by means of a gastrojejunostomy (Fig 6) In 50 per cent of the animals so treated a chronic jejunal ulcer developed immediately distal to the gastrojejunal stoma In another group of animals the pancreatic juice was deviated from the jejunum by anastomosing the pancreatic duct to the terminal ileum In these animals in which the jejunum was protected by the duodenal secretion and the bile, the incidence of jejunal ulceration was increased to 70 per cent. In a third group of animals, the bile was deviated from the jejunum by anastomosing the common duct to the terminal ileum In these animals in which the jejunum was protected by the succus entericus and the pancreatic juice the incidence of jejunal ulcers was 90 per cent In a fourth group of animals, both the bile and pancreatic juice were deviated away from the jejunum by anastomosing the common and pancreatic ducts to the terminal ileum, thus leaving only succus enter

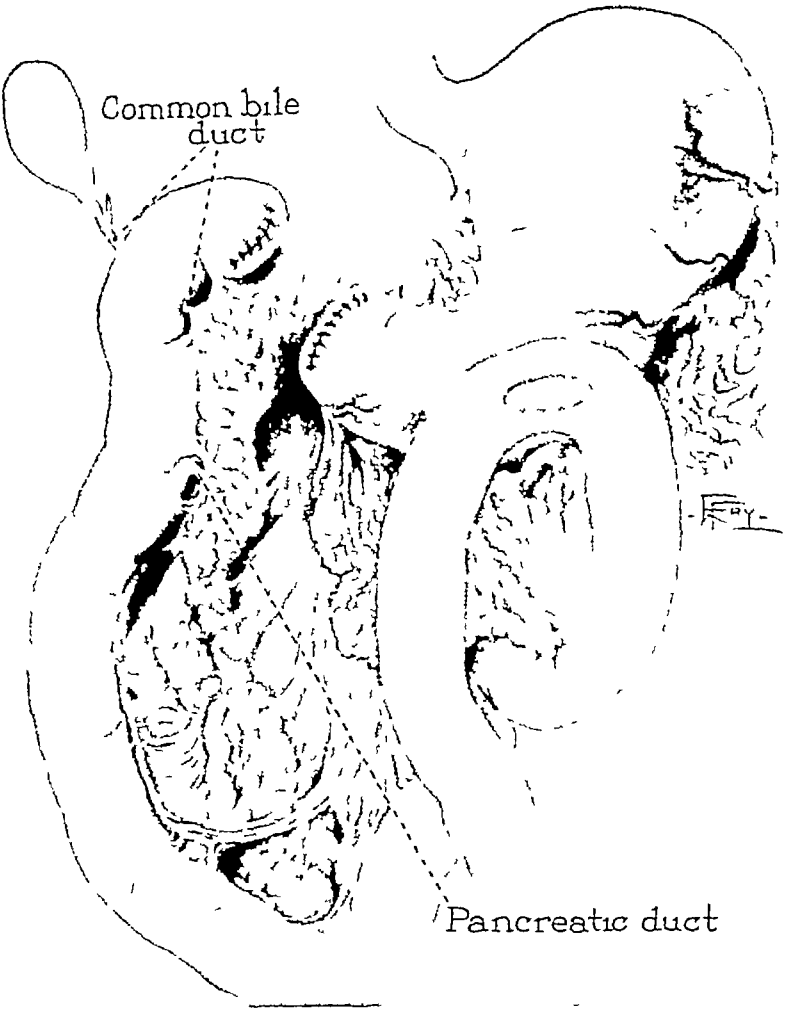

Fig 6 Drawing showing the pyloric occlusion operation The pylorus has been divided, the duodenal and gastric ends closed blindly, and a gastro-enterostomy produced Following this operation jejunal ulcer developed in 50 per cent of animals (After DeBakey Arch Surg, in press)

icus to protect the jejunum Chronic jejunal ulcers developed in 100 per cent of the animals (Fig 7) The susceptibility of the jejunal mucosa to peptic digestion is shown by the results obtained in DeBakey's first group of experiments, as following the pyloric occlusion operation alone ulcers in the jejunum developed in 50 per cent of animals Because the incidence of jejunal ulceration was less in those animals in which the jejunal loop contained succus entericus and bile than in those animals whose jejunum contained succus entericus and pancreatic juice (70 per cent and 90 per cent, respectively), it is apparent that bile exerts more of a protective influence against peptic digestion than pancreatic juice The relatively greater protective influence of bile than pancreatic juice is also shown by the investigations of Berg and Jobling (9) in which following biliary fistulas peptic ulcers developed in 10 of 23 dogs, whereas no ulcers occurred after pancreatic fistulas (8) Mann and Bollman (54), on the other hand, believe that of the three secretions, viz, bile, pan-

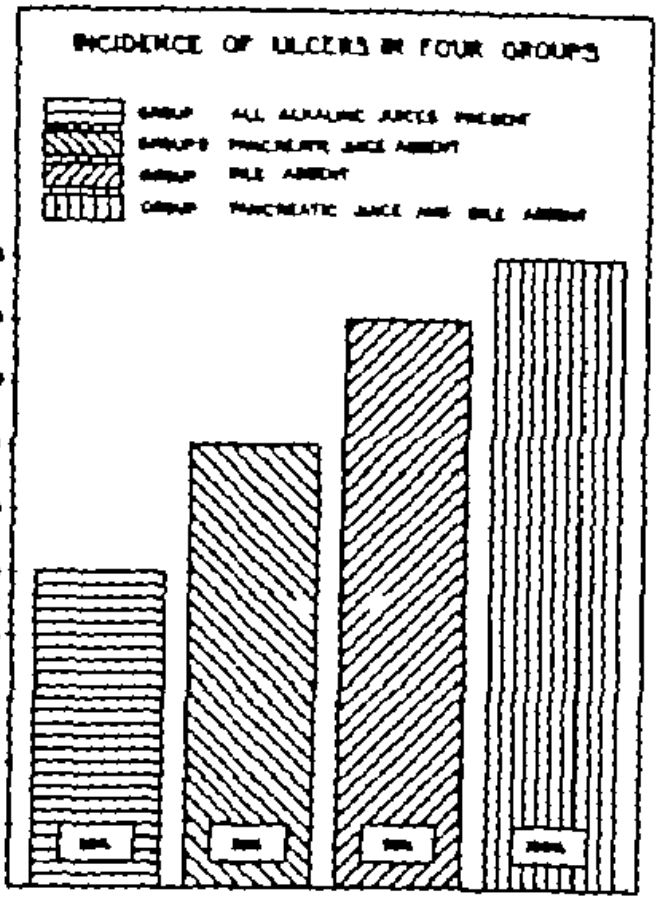

Fig 7 Graph illustrating the incidence of ulcer obtained following the "duodenal drainage operation Group I 30 per cent of ulcers developed following simple "duodenal drainage operation Group II, 70 per cent of ulcers developed when pancreatic juice was deviated away from the anastomosis Group III, 90 per cent of ulcers developed when the bile was deviated away from the anastomosis, Group IV 100 per cent of ulcers developed when both bile and pancreatic juice were deviated away from the anastomosis (After DeBakey Arch Surg in press)

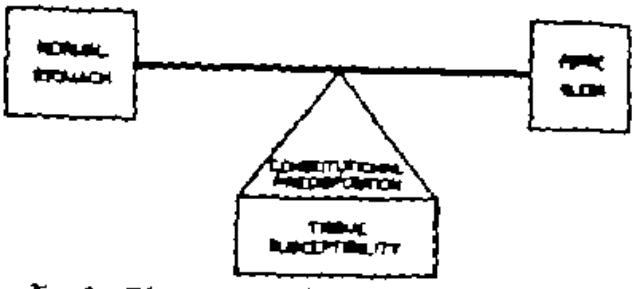

Fig 8 Diagrammatic drawing showing normal balance maintained in a patient with tissue susceptibility and constitutional predisposition Unless there are additional precipitating factors, constitutional predisposition and tissue susceptibility will not produce peptic ulceration

creatic and duodenal juice, bile offers the least protection. In DeBakey s last group of experiments in which the jejunal loop contained only succus entericus, the incidence of jejunal ulceration was 100 per cent illustrating the protective influence of both the pancreatic juice and bile

From these experiments it is obvious that, in the experimental animal at least, which is not liable to develop peptic ulcers two factors are of great importance in the development of chronic ulcers of the upper intestinal tract viz "tissue susceptibility and acidity Certainly in the dog there is no "constitutional predisposition" as exists in humans because Ivy (44) *found only 1 acute gastric ulcer in 900* dogs etherized in the laboratory In the human however as mentioned there are other etiological factors which are important In addition to "tissue susceptibility" which every one possesses, another inherent uncontrollable (as regards therapy) factor is constitutional predisposition." In all probability however most patients with both of these *predisposing factors will have no peptic ulcer* ation unless there are additional precipitating factors. As graphically illustrated in Figure 8, a balance is maintained between normality and peptic ulceration When however in a patient with these predisposing factors there are additional precipitating factors such as hypersecretion and hyperacidity, foci of infection and gastric trauma peptic ulceration results. As graphically shown in Figure 9, the additional predisposing factors disturb the normal balance resulting in peptic ulceration Although hypersecretion hyperacidity foci of infection and gastric trauma, either collectively or individually are responsible for the development of peptic ulceration in a patient with a constitutional predisposition, shown in Figure 9, they are of no significance as regards peptic ulceration in the individual with no ulcer diathesis (Fig 10)

Based upon this conception of the cause of peptic ulcer it is obvious that the therapy of peptic ulcer should be directed along very definite lines Little or nothing can be accomplished as regards the treatment of uncontrollable factors, such as constitutional predisposition and tissue susceptibility " As ulcer diathesis is such an important factor in the causation of peptic ulcer probably the first requisite in the treatment of chronic gastroduodenal ulceration is that the patient be made to realize the existence of his "constitutional predisposition" to peptic ulcer and

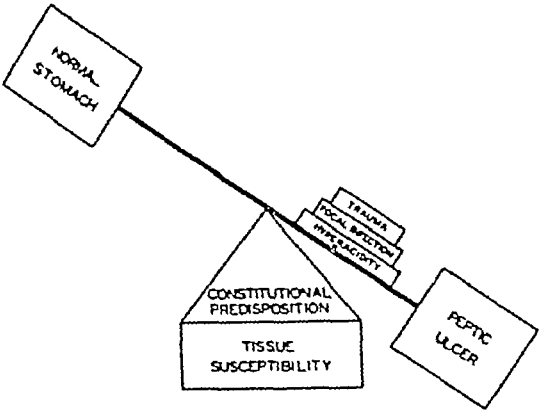

Fig 9 Diagrammatic drawing illustrating production of peptic ulcer in a patient with the predisposing factors, tissue susceptibility, and constitutional predisposition, and, in addition, the precipitating factors, hyperacidity, focal infection, and trauma Following the removal of the precipitating factors, the normal balance is again resumed, as shown in Figure 8, even though tissue susceptibility and constitutional predisposition persist.

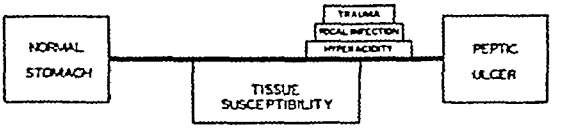

Fig 10 Diagrammatic drawing showing the normal balance maintained even though the precipitating factors, hyperacidity, trauma, or focal infection, are present in an individual without constitutional predisposition Even though the precipitating factors are present, the patient does not develop an ulcer

the necessity of his governing himself accordingly for the rest of his life Although one with an ulcer, potentially will always have an ulcer, a great deal can be accomplished by correcting the controllable, precipitating factors, namely hypersecretion, hyperacidity, focal infections, and gastric trauma Little or nothing can be done as regards the inherent "tissue susceptibility" to ulceration except that the surgeon can refrain from performing those operations in which abnormally susceptible portions of the intestinal tract are subjected to the digestive action of the acid gastric chyme It is obvious, therefore, that in many patients with peptic ulcer the performance of a gastrojejunostomy which permits the bathing of the suceptible jejunum with acid gastric chyme can lead to disastrous results because of the development of jejunal ulcers The reported incidence of jejunal ulceration following gastrojejunostomy for peptic ulcer in humans varies considerably Although Lewisohn's incidence of 34 per cent is probably abnormally high, we are convinced from our clinical experience that the incidence is considerably higher (probably 15 to 20 per cent) than is generally considered by most clinicians Hinton and Church, who report a jejunal ulcer incidence of 16 4 per cent, emphasize the necessity of observing patients with gastro-enterostomy for long periods of time, because not infrequently long periods elapse between the performance of the operation and the appearance of the jejunal ulcer Balfour found an incidence of jejunal ulceration of 3 26 per cent in duodenal ulcer cases treated by gastro-enterostomy, but found none in those in which this operation was performed for gastric ulcer Walton found the incidences of jejunal ulcer following gastrojejunostomy for gastric and duodenal ulcers to be 2 2 per cent and 3 9 per cent, respectively Ryle and Zukschwerdt and Eck believe that 10 per cent of gastrojejunostomies are followed by jejunal ulcers The great frequency of jejunal ulcer is demonstrated by Graham and Lewis' report of 43 cases which they observed, upon 33 of which they themselves had operated

The therapy of gastroduodenal ulceration has not been satisfactory mainly because of the high incidence of recurrences which have taken place largely because the treatment has consisted of attempts to heal the ulcer without correcting the predisposing and precipitating factors In the successful therapy of peptic ulcer the patient as a whole must be treated and not merely the gastroduodenal ulceration, which is only a symptom Although, as mentioned previously, the predisposing or underlying factors are largely uncontrollable, that is, are not amenable to therapy, a great deal can be accomplished by rest and relief from worry The importance of fatigue and worry as causes of peptic ulcer are shown by Barford's observations In 126 cases of duodenal ulcer studied by him, the most frequent cause of aggravation of symptoms was worry (26 cases), whereas the second most frequent causes were overwork and fatigue (14 cases) Psychic and physical rest are important in the

treatment of patients with recurrent peptic ulcer and always should be insisted upon. As little can be done, however to correct the predisposing factors ("constitutional predisposition' and "tissue susceptibility") the treatment of peptic ulcer consists mainly of the correction of the precipitating factors which are amenable to therapy These controllable factors, as heretofore mentioned are hyper secretion and hyperacidity focal infection, gastric trauma, and pylorospasm. Of the various controllable factors, undoubtedly the most important are hypersecretion and hyper acidity The importance of acidity in the causation of peptic ulcer is shown by our experiments as regards the formation of ulcers both in the stomach and in the intestinal tract. As a matter of fact, the treatment of peptic ulcer in the past has consisted largely of measures which decrease or control gastric acidity whether this is accomplished by non-operative or operative means. Because of the etiological importance of gastric acidity it is imperative that the patient abstain from those things which increase the acidity The abstinence must be persisted in throughout the patient s life, because one with an ulcer diathesis has an inherent predisposition to ulceration as long as he lives. We feel that it is imperative that the patient completely abstain from smoking because in our experience, smoking especially of cigarettes, is very detrimental to patients with peptic ulcer Gray (36) found that in a series of duodenal ulcer cases, 96 per cent were smokers, of which 29 per cent were excessive, 31 per cent heavy or continuous, and 40 per cent mild or intermittent smokers. This authority believes that tobacco is one of the principal causes of peptic ulcer Moll and Flint found that smoking increases the secretion of hydrochloric acid in the stomach and tends to produce a hyperchlorhydria. Bandel and Friedrich suggest that the increase in the gastric ulcer incidence in Germany has been due to the concomitant increase in cigarette smoking. Friedrich believes that cigarettes are especially harmful, because most cigarette smokers inhale, thus increasing the absorptive surface eight times, resulting in approximately eight times as much absorption of nicotine. Also the cigarette smoker is likely to smoke between meals when the stomach is empty at which time hyperacidity is especially dangerous. Friedrich believes that the absorbed nicotine exerts a twofold action first, it produces spasm of the blood vessels of the stomach, as he was able to determine by capillary microscopy and, second it increases gastric secretion. The former is due to the direct action of the nicotine on the vessels or due to the increase in adrenalin resulting from the action of the nicotine on the adrenal glands The vasospasm produces an ischemia of the gastroduodenal mucosa which results in necrosis. Seventy-nine and seven-tenths per cent of Friedrich s male patients with ulcer were heavy smokers. The importance of smoking after operation is shown by Friedrich's results Of 34 resections in patients who smoked heavily after operation, although they had been instructed not to do so practically half the patients had symptoms. Of 44 patients who smoked heavily before operation but who limited their smoking to half the amount or even less after operation, only 6 had moderate symptoms, one-seventh of the entire group Smoking was particularly injurious to those patients with gastro-enterostomies. Of 14 patients with gastro-enterostomy who had not limited their smoking after operation only 4 were free from symptoms, whereas of 30 patients who smoked moderately following the operation, 16 were completely free from symptoms. According to Friedrich and L Gray there is less danger if smoking is limited to the immediate period after a meal because during this phase food neutralization will tend to prevent hyperacidity Friedrich states that almost invariably those patients who do not get results following an operation are those *who smoke in the morning before breakfast.* He compares the effects of nicotine on gastric acidity with that which is obtained in animals by sham feeding We are so convinced that smoking, and especially cigarette smoking, is detrimental to the patient with peptic ulcer that we refuse to treat such an individual unless he will totally abstain from smoking Trowell studied the smoking habits of 50 duodenal ulcer male patients and 400 normal men and found 17 per cent non-smokers in

the normal group and only 8 per cent in the ulcer patients Fifty-two per cent of the controls and 78 per cent of the ulcer patients inhaled the cigarette smoke, whereas 44 per cent of the controls and 18 per cent of the ulcer patients did not inhale. Trowell believes that the inhalation of cigarette smoke is an important factor in the etiology of duodenal ulcers and suggests that the detrimental agent absorbed is carbon monoxide Rolleston believes that smoking causes pylorospasm which in turn may cause hyperchlorhydria. On the other hand, according to Barnett smoking is of little etiological importance in peptic ulcer and gastric neurosis

Similarly as with smoking, all patients with peptic ulcer should be strictly forbidden to imbibe any alcoholic beverages because of the definite irritation of the stomach which is produced by them and because of the hypersecretion which results from their ingestion According to Cushny, following the absorption of alcohol into the blood stream there is profuse gastric secretion Because alcohol provokes such marked gastric secretion dilute solutions are frequently used as test meals Although of less importance than smoking and drinking as regards the production of gastric hypersecretion and hyperacidity, condiments of all types should be avoided by the peptic ulcer patient Condiments are detrimental probably in two ways· by increasing the gastric secretion and acidity and by producing gastritis and duodenitis

In addition to preventing increased gastric secretion by avoiding those factors which produce hypersecretion and hyperacidity, neutralization of gastric acidity is of great therapeutic importance Normally, neutralization occurs in a number of ways, but principally by the ingested food and by regurgitation of the alkaline duodenal secretions Frequent administrations of food are essential in the efficient neutralization of the gastric juice and most of the medical therapies of ulcer consist principally of frequent feedings Hurst (43) believes that the neutralizing effect of food is dependent upon its alkalinity Mann and Bollman state that there is "a peculiar quantitative relationship between food and gastric acidity" They have found that "the high acidity of the gastric juice in a dog with psychic secretion was reduced for only 2 or 3 minutes following administration of 20 cubic centimeters of milk or cream, 40 cubic centimeters maintained a reduced acidity for 5 or 10 minutes, but 80 cubic centimeters maintained a low level of acidity for almost 2 hours" Winkelstein (82) found that nocturnal gastric secretion occurs in patients with peptic ulcer, but never in normal individuals (84) He (83) found that the nocturnal gastric hypersecretion can be effectively controlled by the continuous administration (night and day) of food and alkalies through an indwelling gastric catheter On the basis of his experimental observations that following the extirpation of portions of the gastric mucosa ulcers developed only when salivary glands were also removed, Demel believes that the saliva normally exerts a protective influence against gastroduodenal ulcer. We believe that the frequent administration of food, at least every 2 hours until the patient retires at night, is extremely important. Although during the time the ulcer is healing the diet prescribed must be more rigid, it is imperative to impress upon the patient that his eating habits must be changed for the rest of his life If such is the case, it is essential that the diet is liberal enough for the patient to be content with it for such a long period of time We believe that if condiments, roughage and excessive meat consumption are avoided, almost everything else can be taken safely, provided there are frequent feedings and no overfilling of the stomach at any time. *Although we admit the value of the rigid diets suggested by gastro-enterologists during the stage of ulcer activity, we are convinced that much harm can result from the overen phasis of the importance of the relatively short dietary regimen and the frequent disregard for continued dietary discretion* Of great importance also is avoidance of overdistention of the stomach at any time. The patient should be instructed to eat frequently, at least every 2 hours but to eat sparingly at his three regular meals

Although the conservative treatment of peptic ulcer by many internists and gastroenterologists has consisted largely of attempted neutralization of the acid gastric secretion

by the use of alkalies, we believe with Barford that alkalies are of relatively little significance, although if used properly may be of some value. In Barford's series of 160 cases of chronic ulcer the conservative treatment consisted of ulcer diet together with the administration of atropine but without alkalies. During the acute stage of the ulcer and until the ulcer has healed we employ alkalies after meals but feel that the usually employed alkali, sodium bicarbonate, should not be used because, as shown by Lockwood and Chamberlain frequently following the administration of sodium bicarbonate there is a rebound hyperacidity to a point higher than that which was present before the alkali administration. Also as shown by Loevenhart and Crandall, sodium bicarbonate is irritating in high concentrations and is likely to produce alkalosis if taken in excess. These investigators also state that occasionally it causes a precipitation of phosphates in crystal form in the urine, which may give rise to renal colic. Mann and Bollman have also emphasized the limitation of alkali therapy with sodium bicarbonate because of the only temporary decrease in acidity produced by small doses of the sodium bicarbonate and the danger of producing an alkalosis if large doses are used. In our clinical cases we have used calcium carbonate as suggested by Loevenhart and Crandall and have been very well satisfied with the results which we have obtained. According to Loevenhart and Crandall the advantages of calcium carbonate are as follows "(1) When suspended in water it is neutral in reaction. (2) It is therefore only a potential alkali, but it neutralizes the gastric acid to form calcium chloride and carbon dioxide. (3) It can be given almost *ad libitum* If an excess is taken, it passes out in the feces. (4) It apparently has no effect on the activity of the bowel except that, if taken in excess, it increases the bulk of the stool (5) When taken in excess, it will coat over ulcerated areas and may in this manner protect them from the action of irritants." Loevenhart and Crandall found that, in a normal individual 1 gram of calcium carbonate would neutralize the average basal secretion for 7 hours or would neutralize the maximum basal secretion for 1 hour and 40 minutes. We have used calcium carbonate 10 to 20 grains, after each of the three regular meals and in this way have been able to control satisfactorily the acidity in patients with ulcer A decided disadvantage of the magnesium salts, magnesium oxide and carbonate, is that they exert an irritating action on the intestine which, as Loevenhart and Crandall emphasized, is especially undesirable in ulcer patients who frequently have an irritable colon.

The neutralization of gastric secretion by means of mucin, as suggested by Fogelson (30) is of value in many cases of peptic ulcer According to a recent report by Fogelson (31) 63 1 per cent of patients who were considered as having intractable ulcer symptoms became symptom free on mucin therapy Of the remaining patients, 29 4 per cent were benefited by the treatment and 7 5 per cent were not benefited. According to Hurst (43) mucin acts partly by mechanically blocking the mouths of the secreting tubules and partly by its chemical action combining with some of the free acid. He believes that the neutralizing effect is almost entirely due to the sodium bicarbonate it contains. He has shown that in a patient with a hyperesthenic stomach, which is the type usually associated with duodenal ulcer very little mucus is present in the stomach

As mentioned, one of the causes of hypersecretion and hyperacidity is gastric retention, which is caused by an interference with the normal emptying of the stomach. The increased secretion and acidity are partly due to the retention of the normal gastric juice in the stomach, and, as Meek suggested, because of the retention, there is an increased secretion Also the normal regurgitation of the alkaline duodenal secretion is interfered with. The interference with the emptying of the stomach and the normal regurgitation of the alkaline duodenal secretion may be due either to a spasm of the pyloric sphincter (pyloro-spasm) as contended by Ivy and Fauley (46) Finney (29) Judd and Waldron, and Yates, or the absence of normal relaxation (achalasia) as suggested by Hurst (43) Miller (61) Martin and Burden and Deaver and Burden. As there is interference with the

normal relaxation of the pyloric sphincter in cases of ulcer, attempts should be made to re-establish the normal function of the pylorus This is best accomplished by the administration of antispasmodics given in full therapeutic doses Tincture of belladonna given in doses varying from 10 to 20 minims three times a day after meals is usually successful in relaxing the pyloric sphincter By so doing the vicious circle which is set up by gastric retention and prevention of regurgitation of the normal alkaline duodenal secretions together with increased secretion resulting from the gastric retention is corrected In cases in which there is considerable retention and especially in those cases in which there is an acute inflammatory process, the gastric retention must be relieved in some other way, and this is best accomplished by gastric lavage, especially late in the evening An inflammatory reaction about an ulcer will subside very much earlier if stasis over long periods of time with putrefaction in the stomach can thus be prevented Conservatism, of course, is indicated only in those instances in which the mechanical obstruction is due to edema and not due to cicatricial narrowing, because in the former instance the process may subside completely, whereas in the latter the conservative treatment offers nothing

In addition to hyperacidity, another important precipitating cause of peptic ulceration which must be corrected is focal infection As mentioned, focal infections may act in a specific manner by producing a specific lesion in the stomach or the duodenum, the ulcer following the gastritis or duodenitis Such foci of infection are usually in the teeth and tonsils, but may be elsewhere in the body The removal of these foci will, in many instances, bring about complete relief of symptoms in an otherwise intractable case In addition to the specific focal infections, as mentioned, there are non-specific focal infections which are usually located within the abdomen and which reflexly produce pylorospasm which in turn increases gastric acidity Unless these foci are removed and the reflex spasm of the pylorus prevented, relatively little can be accomplished as regards an ultimate cure of the individual The possibility of an inflammatory lesion in the abdomen which may be responsible for a reflex pylorospasm must always be considered and when found the viscus should be extirpated

In order to minimize gastric trauma, which is another but less important precipitating cause, the patient with peptic ulcer should avoid all rough food, such as uncooked vegetables or fruit The importance of trauma from the ingestion of roughage is illustrated by the researches of Ferguson, and of Ivy and Fauley (46) These investigators found that following excision of gastric mucosa a chronic ulcer would develop if the animals were fed rough, irritating food, whereas the ulcer would heal if non-irritating foods were administered

Because of the necessity of treating the patient as a whole in cases of peptic ulcer, the conservative treatment should be used in every case unless there is some complication which requires surgical aid The surgical treatment of gastroduodenal ulceration, therefore, consists largely of the treatment of complications Obviously a patient with mechanical obstruction, with threatened or actual perforation, with repeated hemorrhages or one in whom the possibility of a malignant lesion cannot be excluded, must be operated upon, but each of these conditions represents a complication of the original ulcer Occasionally, but infrequently, an operative procedure may be indicated in an attempt to control the hyperacidity in the patient who is not benefited by conservative treatment Unfortunately, however, the patient who does not respond to a properly conducted regimen of conservative therapy is likely not to respond to operative therapy, as borne out by Emery's observations He reported 4 cases of hypersecretion which were treated by increasingly radical operations Each patient had a high gastric acidity and each patient was worse after the operation than before As a rule, unless there is some definite complication which is an indication for surgical therapy, the patient is probably better off without being operated upon Another fact also remains that every patient operated upon is still a peptic ulcer patient and should continue on the same regimen after operation as he did before operation

The surgical treatment of peptic ulcer consists largely of the correction of the complicating lesion. We feel that every patient who has a chronic callouned gastric ulcer should be given the advantage of an exploration and probable resection because of the great danger of malignant change occurring in this type of ulcer especially if the ulcer is on the greater curvature. Even though the lesion does not appear to be malignant, a subtotal gastrectomy should be done well beyond the confines of the ulcer because it is impossible to tell at the time of operation whether it is malignant or not. Another surgical procedure which is definitely indicated and about which there can be no controversy is gastro-enterostomy in the patient who has had a long standing cicatrizing ulcer in the region of the pylorus associated with gastric retention and hyposcidity. *The results obtained from this operation in these cases are excellent.* The danger of the development of jejunal ulceration in these cases is practically nil because, as the result of the continued gastritis caused by prolonged gastric retention the acid secretion of the stomach is definitely diminished thus obviating peptic digestion of the susceptible jejunal mucosa. The operative procedures which should be done in other cases, those with threatened or actual perforation hemorrhage, or those which do not respond to conservative therapy are not so definite. In perforated peptic ulcers conservative operative procedures are generally indicated. These consist of excision of the ulcer and immediate closure without the performance of a gastrojejunostomy. In cases with hemorrhage we feel whenever possible operation should not be undertaken until after the hemorrhage has subsided and the patient has recovered. In such a case following recovery from the effects of the hemorrhage, extirpation of the ulcer combined with some plastic operation on the pylorus or gastrectomy is usually indicated because a severe hemorrhage generally indicates that the ulcer is a penetrating one which will probably not subside spontaneously under conservative therapy. Occasionally the severe hemorrhage does not subside and even threatens the patient's life. In such an instance partial gastrectomy with removal of the ulcer as advocated by Allen and Benedict, is indicated.

Because of the important rôle which acidity plays in the production of peptic ulcer as evidenced by clinical and experimental observations, and because of the increased susceptibility of the intestinal mucosa to the acid gastric secretion we are convinced that a gastrojejunostomy should seldom, if ever be done in the patient who has a normal or hyperacidity of the gastric secretion. In an individual with ulcer diathesis, gastric hypersecretion and hyperacidity the performance of a gastrojejunostomy is not without danger because it permits the acid gastric chyme to be emptied into the jejunum, which is less resistant to the digestive action of the gastric juice than the gastric or duodenal mucosa. The high incidence of jejunal ulcers in such *individuals is easily explained. As a matter* of fact it is difficult to understand why such a patient with a gastrojejunostomy should ever escape a jejunal ulcer. The reason more do not develop stomachal or jejunal ulcers is probably because a properly performed gastrojejunostomy does reduce the gastric acidity although, as shown by the investigations of Hill and associates, the reduction is less than that obtained by gastroduodenostomy. Granted that partial neutralization of the acid gastric contents follows gastrojejunostomy the operation still remains a dangerous procedure because of the marked susceptibility of the jejunal mucosa unless complete neutralization of the gastric chyme is obtained. As the result of our clinical and experimental observations, we believe that careful gastric analyses are important before any surgical procedure on the stomach is undertaken and we are convinced that in the presence of a hyperacidity or even a normal acidity a gastrojejunostomy should not be done. Because the patient is not only not cured of his ulcer disease by the gastro-enterostomy but also because a jejunal ulcer is infinitely worse than the original gastric or duodenal ulcer any procedure which might be responsible for the development of a jejunal ulcer should be avoided.

A far more logical procedure than the establishment of a new opening between the stom-

ach and the jejunum is some type of operation in the region of the pylorus which will permit a freer regurgitation of the alkaline duodenal secretions into the stomach and thus produce a reduction in acidity The importance of regurgitation of alkaline secretion as neutralizing factors has been shown by the investigations of Boldyreff, Elman and Eckert, Olch, Bockus and associates, and Hill and associates The advantage of such an operation is that it tends to correct a disturbance which exists in patients with peptic ulcer, viz , a dysfunction of the pylorus, and it also retains the physiological relationship of the stomach and the duodenum, so that the acid gastric chyme leaving the stomach first comes in contact with the duodenal mucosa which normally should receive it and which is much more resistant to its digestive action than is the jejunal mucosa Granted that the pyloric dysfunction is either a loss of relaxation or spasm of the muscle, theoretically the most physiological procedure would be excision of the pyloric sphincter, as suggested by Judd (47, 48) and Deaver and Burden The operation consists of excision of a portion of the pyloric sphincter, which will permit emptying of the stomach without retention and also a ready regurgitation of the alkaline duodenal secretion into the stomach in order that neutralization may occur In a recent publication, Judd and Waldron (49), emphasized the importance of excision of from two-thirds to three-fourths of the pyloric sphincter because if less of the muscle is removed than this, recurrence of the symptoms occur They state that the operation has been done at the Mayo Clinic in more than 900 instances and that the only patients in whom there has been a recurrence of symptoms are those in whom adhesions formed between the operative field and the parietal peritoneum or adjacent viscera In these cases recurrence of the pyloric occlusion was not caused by the reformation of the sphincter, but was due to angulation produced by the adhesions The operation is, without a doubt, the most physiological of all the gastric operations, because it disturbs the normal anatomy and physiology of the stomach and duodenum less than does any other procedure If excision of the pyloric sphincter is not feasible for technical reasons, an anastomosis between the stomach and duodenum (gastroduodenostomy) with—Heinecke-Mikulicz, 60, Finney, 28, Horsley, and Judd, 49—or without (Rienhoff and Wilkie) division of the pyloric ring is then advisable, because in this way the emptying of the stomach into the duodenum, which is accustomed to receiving the acid gastric chyme, can be accomplished and at the same time regurgitation of the alkaline duodenal secretion into the stomach can occur Local excision of the pyloric or juxtapyloric ulcers always should be done during the plastic operation, whenever it is at all possible Occasionally, patients with peptic ulcer in whom excision of the pyloric ring, gastroduodenostomy, or other plastic operation on the pyloric sphincter is not possible but in whom there is a hyperacidity and in whom for some reason or another operation is indicated, a subtotal gastrectomy can be done It is an operation which entails a great deal more risk than gastro-enterostomy but the incidence of jejunal ulcer is considerably less because the acid producing portion of the stomach is diminished We believe, however, that unless the ulcer is in the stomach and there is some chance of its becoming malignant, gastric resection is seldom indicated We do not agree with Strauss, Berg (8), and the various European clinicians that gastrectomy is the operative procedure of choice, because the removal of the greater portion of the stomach does not necessarily correct the disturbed physiology which is responsible for the ulceration

CONCLUSIONS

1 The treatment of peptic ulceration has been very unsatisfactory because, in too many instances, attention has been focused on the ulcer itself without the realization that the ulcer is merely a symptom Unless the patient as a whole is treated, the results from therapy are likely to be unsatisfactory

2 The causes for peptic ulcer can be divided into two groups one in which the factors are not amenable to therapy but which are inherent and predisposing, and the others which are precipitating but which are controllable, i e , can be corrected The inherent or predispos-

ing factors are (1) tissue susceptibility and (2) constitutional predisposition. The precipitating factors are (1) hypersecretion (2) hyperacidity (3) focal infection and (4) gastric trauma.

3 Tissue susceptibility which is an inherent quality present in all individuals, is the vulnerability of certain portions of the gastrointestinal tract to peptic digestion, such as the lesser curvature (*Magenstrasse*) pylorus duodenal cap jejunum, and other portions of the intestinal tract subjected to the acid gastric chyme, as Meckel's diverticulum containing islands of gastric mucosa.

Constitutional predisposition, although difficult to define, is unquestionably present in most if not all patients with chronic gastroduodenal ulceration.

4. As the predisposing factors are not controllable i e. are not amenable to therapy the treatment of a patient with peptic ulcer consists of the prevention and the correction of the precipitating factors, hypersecretion, hyperacidity focal infections, and gastric trauma. Hypersecretion and hyperacidity are the most important precipitating factors. The peptic ulcer patient must abstain from those activities which increase gastric secretion and acidity—smoking, especially of cigarettes, ingestion of alcohol and condiments

In addition to the abstinence of those activities which provoke hypersecretion and hyperacidity neutralization of gastric acidity is favored by a diet consisting of frequent small feedings, as food is an important neutralizing agent Alkalies are probably of less value than formerly considered. Sodium bicarbonate is not an efficient neutralizing agent because frequently there is a rebound hyperacidity even greater than that before the administration of the alkali. There is also danger of alkalosis from the use of excessive amounts. The alkali of choice is calcium carbonate. Mucin administration is of value in controlling hyperacidity in many cases. Restoration of the normal function of the pyloric sphincter—relief of pyloric spasm or achalasia by means of antispasmodics—is of importance in the therapy of peptic ulcer because it relieves gastric retention and also diminishes secretion which is stimulated by gastric retention. The relaxation of the pyloric sphincter permits free regurgitation of the alkaline duodenal secretion into the stomach and favors neutralization.

5 All foci of infection must be removed, because they can act either directly by producing a specific inflammation in the stomach or duodenum or reflexly when within the abdomen by producing pylorospasm.

6. In order to minimize gastric trauma, only bland foods containing no roughage should be allowed

7 Because of the constitutional predisposition to ulceration, it is imperative that the patient change his mode of living for the rest of his life, for recurrences can be expected unless the precipitating factors such as hypersecretion, hyperacidity focal infection, gastric trauma are prevented throughout the life of the patient.

8. The surgical treatment of peptic ulcer consists largely of the treatment of complications such as mechanical obstruction, perforation repeated hemorrhages, and danger of malignant change. Only rarely is a surgical operation indicated in those cases which do not respond to conservative therapy

9. In a case of pyloric occlusion with prolonged gastric retention and hypo-acidity gastro-enterostomy is the procedure of choice. However in cases with hyperacidity or normal acidity because of the increased susceptibility of the jejunal mucosa to the acid gastric chyme, gastrojejunostomy should seldom if ever be done because of the danger of the development of a gastrojejunal ulcer In such cases the resection of the pyloric sphincter or the performance of a gastroduodenostomy which permits free regurgitation of the alkaline duodenal secretions into the stomach thus favoring neutralization of the acid gastric contents and at the same time not changing the normal gastroduodenal relationship is to be preferred to gastrojejunostomy The duodenal mucosa is more resistant to the acid gastric chyme than is the jejunal mucosa The chronic calloused ulcer in the stomach which does not respond readily to therapy should be operated upon and radical resection done because of the danger of malignant change.

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Discussion

EMILE HOLMAN, M D, San Francisco Dr Ochsner's comprehensive paper illustrates the inevitable overlapping of the boundaries of medicine and surgery in any consideration of peptic ulcer As Shelton Horsley once said "There must be medical treatment in all cases and there must be surgical treatment in some" Since Boldyreff's original assertion that peptic ulcer is due to a breakdown of the regulation of gastric acidity, overwhelming experimental evidence has been obtained in support of his theory that autodigestion due to increased acidity is one of the most important factors in the development of gastric and duodenal ulcer In this experimental work Dr Ochsner has taken a leading part, and many fundamental facts have been developed in the laboratory by him and his associates

An important factor in the breakdown of the acidity regulation is an altered motility of the stomach characterized most conspicuously by a spasm of the pyloric sphincter The etiology of such a spasm remains obscure but once present it perpetuates a vicious circle which inevitably leads to chronic disorder Hughson's experimental observations suggest that the initial instigator of the pyloric spasm may be an inflammation of the peritoneum He observed pylorospasm and a marked delay in the emptying time of the stomach following a localized peritonitis anywhere in the abdomen Clinically, such an inflammation may have its seat in a diverticulitis, an appendicitis, a cholecystitis, or even a salpingitis You are all familiar with the long existing clinical presumption of a relationship between these conditions and duodenal ulcer Such peritoneal irritation does not, however, account for all cases of pylorospasm, and we are forced into acknowledging a nervous origin of the spasm, initiated, according to Cushing, by central stimuli, or perhaps having its inception in a hyperactive sympathetic system acutely attuned to an environment productive of mental strain, mental irritation, and mental fatigue. It is highly probable that such a pylorospasm is the first factor in the vicious circle of pylorospasm—decreased gastric motility—gastric stasis—hyperacidity—ulceration, rather than the sequence of hyperacidity—pylorospasm and ulceration as suggested by certain authors

Granting that pylorospasm may be an important factor in the development of hyperacidity and ulceration, the only truly physiological operation, following failure of systematic medical care, would be complete excision of the pylorus by the so-called Billroth I operation or a modification of it The Finney, Judd, and Horsley pyloroplasties aim to eliminate the pyloric sphincter by partial excision, but experience indicates that such partial excision is occasionally ineffective, and not always applicable, and we believe complete excision of the pylorus to be more physiological and therefore more effective Such a procedure obviates the inherent objection to any form of gastrojejunal anastomosis, namely the flow of unmodified gastric juice directly over the jejunal mucosa, and it also provides for the easy reflux of biliary, pancreatic and duodenal alkaline secretions into the stomach, which Boldyreff considered so essential to the normal acidity regulation of the gastric secretion We believe the division of circular fibers of the duodenum and stomach, which in the Finney, Judd, and Horsley pyloroplasties is inevitable, leads to local visceral paralysis and stasis and may interfere with this unhindered reflux of duodenal contents into the stomach

The operation of simple gastrojejunostomy in the presence of hyperacidity cannot be condemned too strongly and should be employed only in the presence of a proven anacidity or hypo-acidity

Certain mechanical considerations are of major importance when a gastro-enterostomy is contemplated The disturbed motility of the stomach or duodenum in the presence of an ulcer may produce not only a pylorospasm, but may produce also a spasm of the gastric or duodenal musculature opposite the ulcer When these spasms occur simultaneously, there results a distention of the visceral segment between the ulcer and the pylorus, and it is suggested that this distention is responsible for much of the epigastric discomfort of peptic ulcer Any operation which fails to prevent such distention of the segment lying between the ulcer and the pylorus may well fail to correct the epigastric discomfort incident to the ulcer

Dr Ochsner suggests that in the diet one omit roughage and uncooked fruit and vegetables Patients invariably object to such a diet because it promotes constipation and because of its monotony Their hunger for something fresh is very real and sometimes overpowering It would seem that it is a question not so much of adhering to a diet without roughage as it is a matter of eliminating from the diet some chemical element capable of exciting gastric secretion and of provoking such discomforts as heaviness, epigastric gnawing, and regurgitation Cantaloupes, watermelons, fresh pineapples, apples and berries excite these difficulties On the other hand, scraped banana, fresh prunes, persimmons, peaches, and ripe blackberries are usually well tolerated Similarly, lettuce, tender celery, and fresh carrots unadorned by spices and sauces usually produce little discomfort, and are a source of vitamins so necessary for normal well-being

It is a pleasure to be able to endorse heartily Dr Ochsner's admirable paper

FUNDAMENTALS VERSUS GADGETS IN THE TREATMENT OF FRACTURES[1]

PAUL B MAGNUSON M D F A C S Chicago, Illinois

THERE is a passage in the Bible which in part reads "This is an evil generation. They seek a sign and there shall no sign be given." In the fear that the statements made herein may lead some to think that I am of the opinion that this is an evil generation of surgeons, I hasten to state that this is quite contrary to the fact. Progress is achieved through the ideas and work of many men. It is necessary however to sift these ideas and take the good out of any or all and throw aside whatever is not adaptable to our purpose. A sign, a cure, a panacea, which will bring good results for our patients has not yet been given.

Each person is an individual and differs from all others, consequently each case must be considered a law unto itself Fractures do not differ from other conditions in this. Although fractures are mechanical and tangible things, an apparatus will not do in one case what it has done in another A new method of treatment is not necessarily good It may have worked wonders in one case and in the hands of its originator but may be a total loss in another similar case. In these days of mechanical advancement, we see many devices of strange and wonderful design advocated for the reduction and retention of fractures. Some are very ingenious applications of standard appliances to meet a condition which has arisen in a given case, some are strange and mechanical contrivances which it would take a Philadelphia lawyer and a mechanical engineer to apply They might work if one could apply them with nothing to bother about but mechanics but many devices do not take into account the anatomy and physiology of the parts to be treated and consequently cannot be used successfully in any but the unusual case. Such apparatus confuses and in the maze of mechanical gadgets the *principles* of treatment of the individual fracture in hand are overlooked and forgotten. There can be no objection to devising an apparatus which serves to answer a need in any case but to the average surgeon it would be much more useful if it were presented as the application of a principle.

Fractures are not new in the field of surgery Records of fracture treatment are in existence which were written 4500 years ago The Edwin Smith surgical papyrus, of which the late Dr James R. Breasted professor of Egyptology at the University of Chicago, recently made an admirable translation, is apparently a collection of case histories extending over several centuries, and dating back to the 5th Dynasty The distinguished gentlemen who delve into Egypt s past dispute among themselves the approximate date of the different dynasties, but are in apparent agreement that the 5th Dynasty reigned in Egypt at least 4500 years ago. Dr Breasted and Dr G Elliot Smith, professor of anatomy in the Egyptian Government School of Medicine, have made some interesting observations on mummies exhumed in recent years. Breasted says that between 5000 and 6000 bodies were examined and that one in every 22 showed a fractured bone. Splints have been found still in place, but Breasted says that such cases must have succumbed soon after injury as no evidences of healing are seen. Fracture of both bones of the forearm was frequent, due to the custom in Egypt, then as today of fencing with heavy sticks. These fractures were treated logically and the results, according to Smith were excellent. The bark of a tree, supposedly the acacia, was molded carefully around the fractured arm from the base of the fingers to the elbow and was well padded around bony points with folded linen. In 100 cases studied many of which must have been compound, only one showed signs of suppuration.

Fractures of the femur did not fare so well Splints were applied which immobilized the lower fragment including the knee and ankle but extended only a few inches above the level

[1] Fracture studies presented before the Clinical Congress of the American College of Surgeons, San Francisco, October 28-November 1, 1935

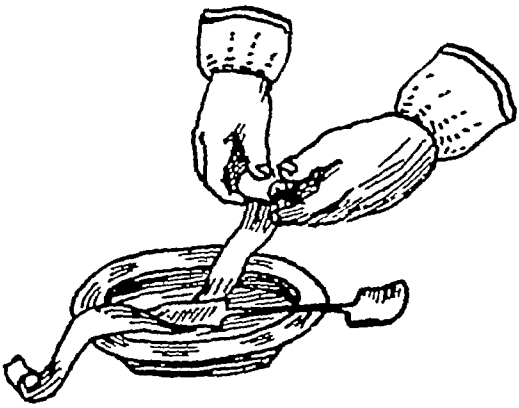

Fig 1 Waxing a bandage Double spatulas of the form shown are found among ancient Roman instruments from Pompeii (After Scultetus)

of the fracture The results, as might be expected, were poor, and many show considerable shortening, displacement of bones, and exuberant callus Not infrequently a case is brought into the accident ward today splinted with as little thought and understanding in exactly the same way, and we are inclined to wonder whether, after all, we have progressed far since the days of the Pharaohs

Our next historical evidence of the treatment of fractures dates to the time of Hippocrates, the Father of Surgery as well as of Medicine In his three books wherein fractures and dislocations are considered, the fundamental principles in the treatment of fractures which he describes might find a place in the most modern textbook These differ little from the generally accepted methods of today except from the standpoint of open reduction The keynote of treatment 2500 years ago, as now, was traction and countertraction, so far as we know the Greeks did not apply suspension with continuous traction and countertraction, but they very apparently did take into consideration the constant displacing effect of muscles The equivalent of our plaster cast was made by passing strips of thin cloth through melted wax, which hardened, the bandage was bound around the fractured limb while traction and countertraction was maintained (Figs 1 and 2) These casts were reinforced with splints applied outside the cast and bound to it (Fig 3) Traction and countertraction was

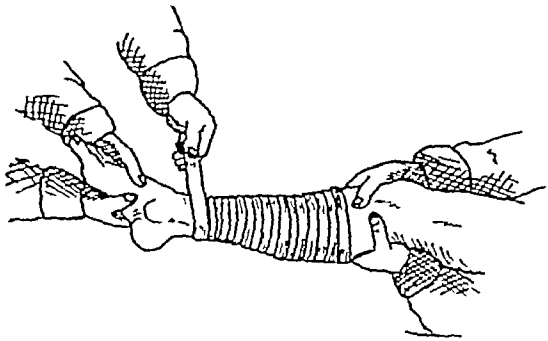

Fig 2 Second waxed bandage fixed over the site of fracture and carried downward for several turns, preparing to return upward and end at the top of the first bandage (After Scultetus.)

maintained by well padded wooden cuffs cut to fit at suitable points above and below the fracture, the cuffs were then held apart by rods of wood which acted as a straight spring Hippocrates says that these bands must be well padded at bony points "as tissue dies beneath a constantly maintained pressure" He emphasizes this time after time (Figs 4 and 5)

Apparently the reduction of fractures and dislocations was well understood, and many ingenious and powerful appliances are described for the use of the surgeon The glossiconium for the reduction of fracture of the femur used pulleys and a windlass to exert the force necessary to overcome the powerful muscles of the thigh, this force being applied through strips of cloth put on the thigh in the form of a clove hitch (Fig 6)

Incidentally, not so long ago this same hitch was described by Collins and since then it frequently has been referred to as the Collins hitch, but Hippocrates had described it as

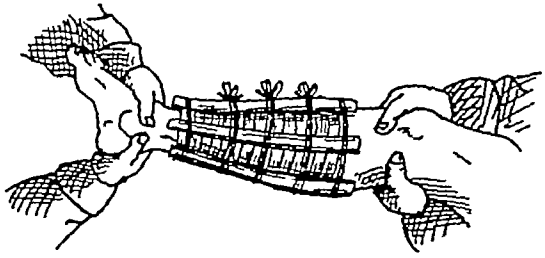

Fig 3 Applying the splints on the seventh day First the two bandages have been put on, then the waxed pads, the bandaging to fix which can be seen under the splints. (After Scultetus.)

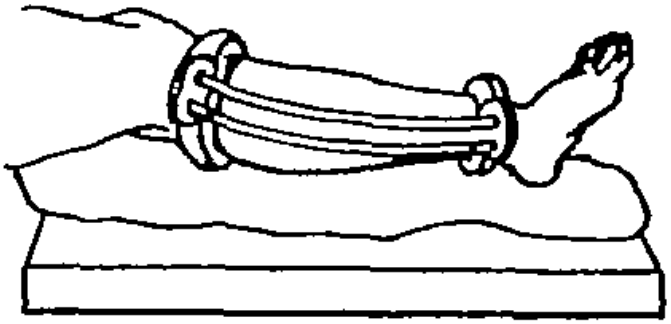

Fig 4 Splint for leg fracture described by Hippocrates. Made of elastic rods fitting into loops on shackle-like pads above the ankle and below the knee (After Littré.)

being an old form of knot which had been used by sailors for many years, and called attention to the fact that it would not slip.

There were fracture tables and portable fracture tables with perineal rests, ratchets, screws, levers and windlasses, and Vidius calls attention to the fact that the perineal rest must be well padded to avoid damage to the soft parts against which it presses (Fig 7)

The scamnum described by Vidius for obtaining traction and countertraction embodies the same general principles. Hippocrates describes a fracture box (Fig 9) although he does not advise its use.

Hippocrates says that the man who presumes to treat fractures must be equipped to do so under any conditions. The men in the larger cities should have the heavier equipment which has been described but the men in the smaller communities and the traveling doctors must adapt whatever they have at hand to fit their needs. He describes a fracture table improvised from a ladder such as might be found in any household by which

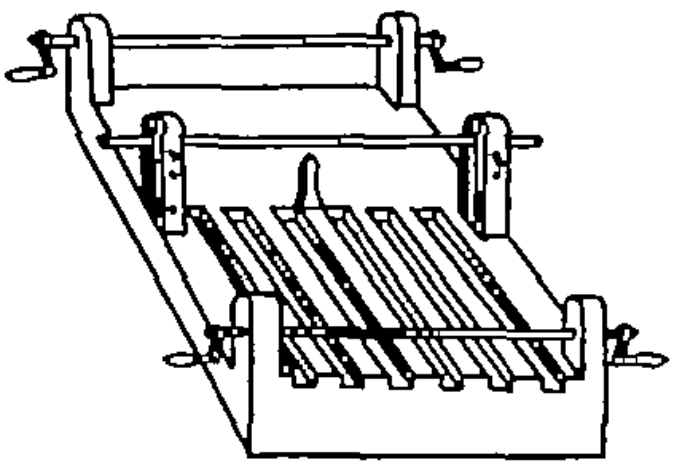

Fig 7 The scamnum of Hippocrates (After Littré.)

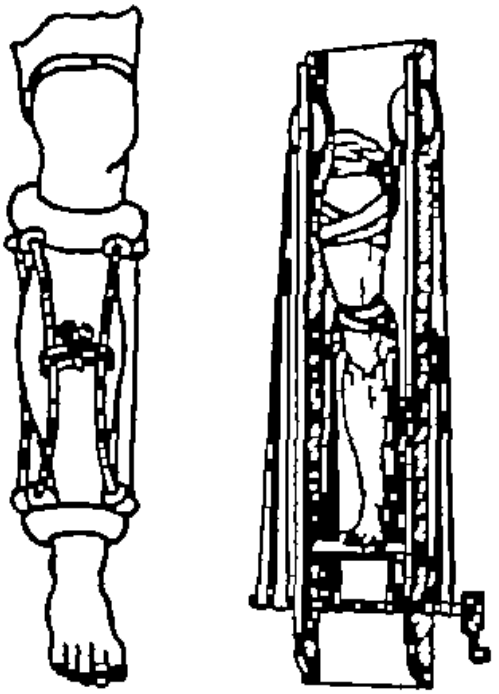

Fig. 5, left. Top view of same to show the tying together of the two top rods

Fig 6. The glossocomion of Galen, applied for fracture of the thigh. (After Vidius)

the same traction and countertraction may be exerted (Fig 10) For instance, in fractures near the elbow traction is applied by means of a clove hitch attached to the wrist. This in turn is acted upon by the system of pulleys seen in the illustration Countertraction is

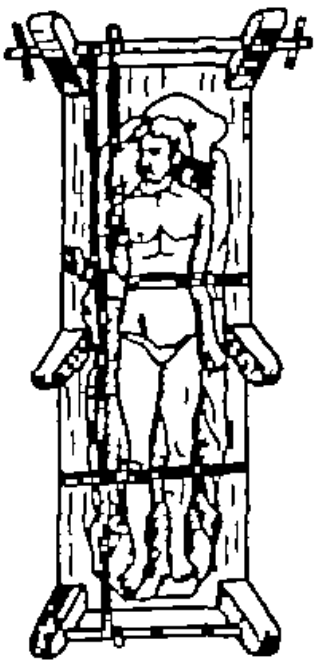

Fig. 8. The scamnum in dislocation of the elbow (After Vidius.)

Fig 9 Box splint or "canal" (After Scultetus)

maintained by a rung of the ladder pressing firmly in the axilla on the injured side Similarly, in reducing a fracture of the lower limb, the extension is applied by a clove hitch and counterextension by bands passed between the thighs and attached to the upper end of the table so the patient may not be displaced by the powerful pull necessary

It is quite evident, therefore, that even in those days there were many methods Hippocrates urges the practitioner to use the method which is best fitted to reduce the type of fracture with which he is dealing, and if one method does not work to try another In his third book he cautions that "*extension of fractured or dislocated bones is not to be delayed to the third day but is to be carried out on the first day,* that slings may be used for some fractures in the upper extremities, but in the lower extremities fractures must be maintained by splints, that there must necessarily be great distinction drawn in the prognosis between simple fractures and compound fractures, that the alinement of bones must be regulated according to nature, that the line of the hand and arm in fracture of both bones of the forearm should be carefully studied, the forearm should be at right angles to the upper arm, but in fracture of the leg the straight position is preferable, that movement must not be allowed until the fracture is solid; and that extension must be made and maintained in a straight line"—that is, in the long axis of the bone He says that the extension should be most powerful in the thickest bones with the greatest flesh, or in the forearm, having recognized that the muscles of the forearm are more irritable and active than many others of like size and bulk He also calls attention to the fact that elevation reduced swelling, that in compound fractures it is impossible to tell

Fig. 10 Reduction of both bones of the forearm at elbow.

whether the bones will heal or whether the fragments of flesh and bone will be detached He cautions that the fragment of bone which protrudes and is loose should be sawed off because it will die, will be extruded, and will prolong the convalescence, that if the flesh is completely torn from the bone it will die and become dried and exfoliate Also we see that five centuries B C the statement is made "When a bone is broken fairly across it is more easily treated, but when broken obliquely it is more difficult to manage" For the most part, Hippocrates says, in the case of the clavicle there is little disability resulting, but there is practically always a lump at the point of fracture The differential diagnosis between a dislocation of the acromioclavicular joint and a fracture of the clavicle is also clearly made

Prognosis as to time of healing is much shorter than would be given today Hippocrates says that 40 days for fracture of the humerus can be expected, but if the fracture is not healed in that time the patient should be kept on a stricter diet for a longer space of time, he does not describe the diet, however He cautions about frequent examinations, especially of the bones of the forearm, and says that when they are once put in place they

should be left there and not disturbed. He puts the period of convalescence at 30 days, but adds that there is nothing precise about this matter "*for one constitution differs from another and one period of life from another*" With regard to the femur he says nothing should be omitted in order that the parts may be properly extended and put in a straight line, for says he, it is a matter of great disgrace in an injury to exhibit a short thigh. In the arm where shortening might be concealed the mistake might not be noticed, but a shortened thigh bone would exhibit the man maimed. All these principles were laid down more than two thousand years ago before anatomy and physiology were known. What keen observations and clear recording for colleagues and for posterity!

This knowledge recorded by Hippocrates was carried to Rome along with other Greek culture. Medicine and surgery was not a popular vocation among the ancient Romans. Theirs was a mercenary semi-civilization, and medicine did not offer in those days, any more than now too much compensation for the time, skill, and labor involved in its study The majority of the noted surgeons of the day were Greeks, either slaves or freemen. Celsus, though not a medical man, compiled a huge encyclopedia of the then current knowledge, most of which had come from Greece. In the first century A.D., Martial referred to the fact that Hermes was recognized as the best surgeon for fractures, and remarked that there were many specialists, some for enlarged tonsils, some for the removal of brands from slaves, etc.

Galen, 130 to 200 A.D makes three commentaries on Hippocrates account of fractures and offers some suggestions from his own experience, which doubtless was extensive, inasmuch as he was surgeon to the gladiators. A recently discovered statue, presumably dating from the time of Galen, represents the partially dissected body of a Gibraltar ape, the anatomy of which, as we know differs little from that of the human body It may be assumed that not only Galen but his predecessors as far back as Hippocrates and even farther studied anatomy in this manner although in ancient Egypt the destruction of the body meant the destruction of the soul also. It does not seem possible that Hippocrates could have gained his knowledge of the anatomy of the body without the aid of dissection, and after all, there were plenty of slaves and criminals in those days, in whose bodies no one had any particular interest, and in their souls, less.

From the fall of the Roman Empire in the 3rd and 4th centuries A.D the long period of the Dark Ages of Europe intervened until the dawn of the Renaissance, and during this period nothing of note pertaining to fractures was written or described. The Church, always jealous of its perquisites, was responsible for the practice of medicine as a whole and guarded its secrets, and while there must have been many fractures in those centuries of almost incessant warfare, nothing of importance appears to have been recorded. An Arabian authority in the 10th century emphasized the importance of crepitus in the diagnosis of fractures, and at about the same period another authority advised sawing off the ends of fragments in non-union and described fractures of the spine resulting in paralysis. The science of medicine in the East far outstripped that of the West. Europe was peopled with barbarians during that period and the culture and enlightened ideas that brought her out of the Dark Ages were an importation from the East by the Crusaders. Previously the Moors, who conquered Spain, had brought much of the ancient knowledge of the East with them. The great Alexandrian Library probably provided the basis for their medical culture.

In the 15th century the barber surgeons of France were given an examination on the care of fractures and dislocations, which incidentally was conducted in public before the mayor and other dignitaries. What the mayor knew about fractures no one has disclosed Paré's work in the following century is well known, but it was Vesalius, whose work was published in 1543 when he was only 29 years of age, who laid the basis for our present understanding of anatomy However for many years fractures and dislocations were cared for mostly by bone setters, although the army surgeons had considerable experience. I am

unable to find any understandable description of the methods of the bone-setters, or any reasons for their doing what they did In England and Wales the profession apparently was hereditary in comparatively modern times Watson has recorded eight consecutive generations of bone-setters in Wales The paternal great-grandfather of Hugh Owen Thomas (1735–1814) was apparently the most celebrated and skilful A generation later there were 21 practitioners in the Thomas family, representing both sexes Evan Thomas, the father of Hugh, set up as a bone-setter and practiced among the neighboring farmers In this country the Sweet family of Rhode Island was famed for their skill as bone-setters, and Comstock recorded that one of them successfully treated DeWitt Clinton of Erie Canal fame, after 52 physicians and surgeons had failed That fracture must have been treated by all the doctors in Rhode Island and some from neighboring states, and the bone-setter probably had as good a press agent as a certain foot-twister of today

The first modern book on the treatment of fractures and dislocations was written by Sir Astley Cooper in 1822, and by 1839 this publication had had 10 editions This work undoubtedly was responsible for the revival of interest in the treatment of fractures, at least in this country In 1827, Nathan R Smith devised suspension in fractures by the long anterior splint and in the same year J Kearney Rodgers was the first to wire ununited fractures successfully, although it had been attempted in 1805 by Moreau in France Two years later Daniels, of Georgia, published his work on weight and pulley traction for fractures of the femur, which he had been using since 1819 This is the first record of suspension Barton wired fractures of the patella in 1834 Detmold began drilling ununited fractures in 1850, and Brainard of my own city followed him 4 years later In 1857 Van Ingen advised elevating the foot of the bed to make the body act as countertraction in fractures of the femur, in addition to Daniels' weight and pulley Buck's well known extension appeared in 1851, and Hodgen's equally well known splint appeared in 1863 In the previous year, Hunt, of Philadelphia, introduced sandbags The starch bandage was invented in 1840, and the plaster-of-Paris cast by Mathieson, an army surgeon of Holland, about the same time How many sleepless nights were spent, and how many needless gadgets were invented *before* these steps is not recorded, but worthwhile ideas do not usually spring full blown from the brow of the gods

John T Hodgen, who was a graduate of the University of Missouri, a general practitioner and afterward surgeon general of Missouri, had a decidedly mechanical turn of mind, and undoubtedly was far in advance of the current practice of his day He emphasized the extreme folly of urging any specific apparatus in the treatment of fractures of any particular bone, and said it was too apparent "to require a remark in refutation" With reference to his famous splint, he said it was a modification of the wire splint of Smith and Swinburne's extension, with his own strip bandage supports used in the cradle splint

In the 1860's Hugh Owen Thomas described the splint with which we are all so familiar He had established himself in the great port of Liverpool, where he came to be surgeon for 28 labor unions It was in this practice that he gained his vast experience in the treatment of injuries, especially fractures My former teacher, Professor John Ridlon, one day counted 160 cases coming to Thomas' clinic Sunday was set aside for his charity clinic. He had no hospital appointments and his splints and many other forms of apparatus were made and fitted on his premises Probably he did more work in this line than anyone of his generation, and his pupil, Sir Robert Jones, until his death carried on the work and ideals of his teacher In the treatment Thomas stressed the importance of enforced, uninterrupted and prolonged rest He pointed out that the circular compression induced by plaster interfered with the true conception of rest hence, in 1867 he devised his famous splint, which today I believe is adaptable in original or modified form to the proper treatment of more fractures of the long bones than any other splint ever invented I say this without fear of contradiction It can be used in the reduction of fragments and also for

their maintenance in reduction. It can be adapted for suspension or ambulatory treatment, and when properly used is of the greatest service.

In 1895 the discovery by Wilhelm Konrad von Roentgen of the ray which bears his name marked the next great step forward in the diagnosis and treatment of fractures. Robert T Morris, of New York, said When the X ray came into use as a diagnostic resource, it was for surgeons what a stereoscopic view of the soul would have been for the theologians. It was the X ray that taught us the difference between anatomical position and a functional result. We worried overmuch when the picture showed the ends of the bone out of complete contact, and forgot that these ends had wonderful ways of uniting in those days prior to the time the X ray permitted us to see them. I want to add, however that this does not preclude the desirability of an ideal anatomical result, because undoubtedly there is a larger percentage of good functional results when the fragments are brought into anatomical re-position than when there is some degree of overlapping or misalinement.

The section on surgery of the British Medical Association in 1910 recommended a report on the ultimate results obtained in the treatment of simple fractures with or without operation and this review embraced a period from January 1906 to December 1910. There were gathered from 20 hospitals throughout the United Kingdom, 1016 records of patients under 15 years of age, and 1580 records of patients over 15 years of age. Good results were obtained in 45.4 per cent of the cases without anatomical re-position but in 66 3 per cent of cases, good functional results were obtained by anatomical re position. The conclusions were that no method, either non operative or operative, which does not definitely promise a good anatomical result, should be accepted as the choice.

The report says that mobilization and massage by themselves have not been found to secure a high percentage of good results they are, however valuable supplementary methods. Methods which secure re-position and absolute fixation of the fragments yield better results than those which fall short of this. Imperfect fixation by wire or other suture has been found unsatisfactory for long bones, except in cases in which the olecranon process is involved. The conclusion is followed by the statement that *operative treatment should not be regarded as a method to be resorted to after failure of non-operative measures and that to secure the most satisfactory results from operation it should be employed as soon as possible* but it must be appreciated that operative treatment requires special skill and experience, and in addition such facilities as will assure asepsis. A considerable portion of the failures recorded were due to infection.

Great stimulus was given in this country to the operative treatment of fractures by the visit, in 1910 of Sir Arbuthnot Lane, and for a number of years following there was promiscuous fixation of fractures with Lane plates by persons who had had no training in the treatment of fractures or in surgical technique. The result was the frequent occurrence of osteomyelitis due to infection following operative treatment of fractures employing fixation by steel plates. This is still one of the favorite forms of fixation. Unquestionably it is applicable to certain cases. Probably the reason for its popularity is not that it is the method of choice in most instances, but because the application of the plate is easy and requires small outlay for equipment, and little skill. One needs nothing but a plate, some screws and a screwdriver a will to operate, and sometimes, it is to be feared, a lack of conscience and an absence of a feeling of responsibility for the end-result. I once asked Dr John B Murphy how many Lane plates he removed, and his answer was "Eight out of every ten I put in and I don t know who takes out the other two. It would seem that a method which necessitates two operations and the insertion of an irritating material could in many cases be avoided and certainly to make an incision over a bone which lies close under the skin and place a foreign body immediately under the incision—and this is not infrequently done—does not display good surgical judgment. So here again we have a question of experience and judgment in the use of a valuable method, but a method which is to be selected for the individual fracture.

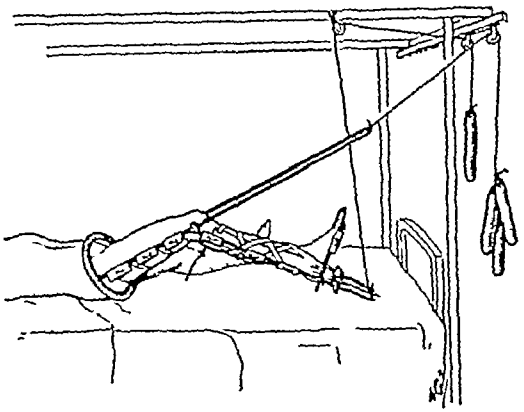

Fig 11 Skeletal traction applied through the lateral and crucial ligaments Traction on the end of the Thomas splint and points of pressure on the calf near the upper end of the tibia.

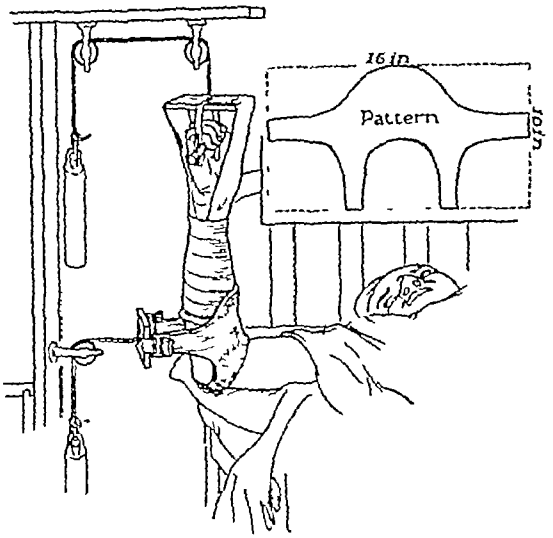

Fig 12 Skeletal traction through the lateral ligaments of the elbow applied through the upper forearm to the lower end of the humerus

In 1909, Steinmann demonstrated his famous nail, by means of which traction could be applied directly to the bone During the great war, however, calipers were devised to take the place of the Steinmann nail, which has this handicap should infection occur in the presence of the nail it may extend into the tunnel through which the nail is driven, a tunnel of infection through the middle of a bone is not easily handled and may result in permanent damage By means of calipers the same skeletal traction can be secured and in some cases with some advantage over the nail, and should infection occur it is usually localized to the surface points of contact instead of going through and through This does not mean, however, that the Steinmann nail is not the method of choice in some cases

Kirschner's wire was introduced in 1909, a method of skeletal traction exerted by piano wire stretched tight and held in a U, through which traction could be maintained This many times has proved to be a great advantage over both calipers and Steinmann nail No preliminary drilling need be done because the wire acts as a drill, and there is less likelihood of infection because the foreign body introduced into the bone is small Kirschner wire, in my opinion, has been one of the greatest contributions to the treatment of certain fractures that has appeared in the last generation Skeletal traction may also be maintained on the femur by traction through the lateral ligaments of the knee (Fig 11, femur) and on the humerus through the ligaments supporting the elbow, if these joints are flexed and pressure is applied close to the flexion angle (Fig 12, elbow)

The vast development of industry and high speed transportation has brought about a tremendous increase in the number of fractures in the last 25 years Since the advent of the automobile, even during the early days of 15 and 20 miles an hour speed limits, we have encountered many unusual types of fracture unknown to our predecessors In 1917, Dr Scudder established a fracture service at Massachusetts General Hospital Five years later, realizing the tremendous disability caused by improper treatment of fractures, and the lack of understanding of fractures which were occurring with greater frequency, he called a conference in Boston, attended by 25 surgeons, and out of this conference grew the Fracture Committee of the American College of Surgeons, which was established in 1927 with Dr Scudder as chairman This committee has worked for the enlightenment of the profession to the end that fractures would be treated more intelligently and that there would be improvement in results The committee has established standards for

equipment in hospitals, and, wherever possible, has persuaded the hospital staff to install a special fracture service to be headed by men especially interested in, and equipped to treat, fractures from their inception. Fractures, however do not always occur under conditions to bring them within the intent of the Committee they have a tendency to occur at inopportune localities. A large percentage fall into the hands of doctors who have not mastered the fundamental principles underlying treatment. The terrific violence which causes many of these injuries has produced many new and hitherto unheard of fractures—fractures which the textbooks cannot describe, because each one is a law unto itself and must be treated as such.

Fractures are mechanical in origin, and are controlled by mechanical factors, and the man who undertakes the treatment of fractures should have a thorough knowledge of mechanics, the fundamentals which underlie the production, the reduction and the retention of the fracture at hand, and the reason for applying the mechanical means of maintaining the fragments in position Unless the surgeon has an understanding of the anatomy and the physiology of the parts as well as the pathology he will continue to treat fractures by somebody's method. Fractures never have been reduced by brawn without a liberal mixture of brains. We have had innumerable kinds of apparatus invented and described for the reduction of fractures and if one were to have one-tenth of it in his equipment he would spend half his income and might be able to use only one piece a year to advantage. Splints have been devised that look beautiful in the picture—shiny and efficient with many straps and buckles—but when applied, frequently it is found that the straps do not give support in the right place and the splint cannot be held at just the particular angle necessary to fix that particular fracture in the most favorable position. The soft parts cannot stand the pressure the patient is too fat or too thin or the splint will not stay in position for one reason or another Traction and countertraction are difficult to maintain, and in ambulatory treatment practically impossible, and when it is necessary to maintain these the patient should be in bed. Because a patient can walk around with a fracture of the arm is no reason why he should be allowed to do so Suspension with traction and countertraction is still the most valuable form of treatment, and when I say suspension I do not mean traction and countertraction alone. I mean suspension which allows freedom of motion of the body as a whole while still maintaining the line of traction on the fracture.

Boehler's work has given great impetus to the use of many forms of mechanical apparatus particularly to the skin-tight cast In the hands of Boehler they are undoubtedly excellent. Boehler knows how to choose the case to which his methods are applicable. But when one sees an attempt to maintain traction in a straight line on a fractured femur by means of an apparatus which rests on the bed while the patient tries to change his position or allow usual nursing care, the lower fragment fixed to a support which rests on the bed and the upper fragment fastened to the body which is not fixed, one is inclined to wonder whether the surgeon understands what he is attempting to do This is what happened in the ancient Egyptian cases previously mentioned the lower fragment is well immobilized up to the point of fracture and the upper fragment is allowed to ride free and engage in all motions in which the body engages When one sees five Kirschner wires driven through an extracapsular and intertrochanteric fracture of the femur up into the hip, to maintain a fracture in position which could easily be maintained by traction and abduction, he wonders whether gadgets are not taking the place of good sense.

Ridlon observed that Thomas success was due to the application of right principles rather than to the use of this or that apparatus, this corresponds to the opinion of Hodgen, and to the teaching of my old friend Dr G G Davis, of Philadelphia. Dr Davis was one of the greatest anatomists of his time, and from his teaching his pupils gained an insight of anatomy far beyond the abstract—they saw a living, pulling bending, circulating, sensitive anatomy where one looked at the skin and saw beneath it the fascia, the muscles, the ligaments, the bones, their interrelationship,

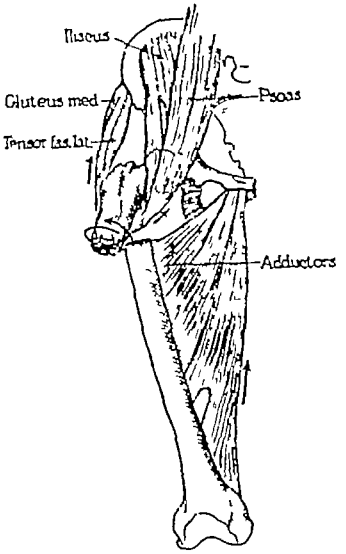

Fig 13 Diagram of muscle pull controlling fracture of the femur at or near the junction of the upper and middle third, illustrating the principle "the fragment which can be controlled should be brought into alinement and rotation with the fragment which cannot be controlled"

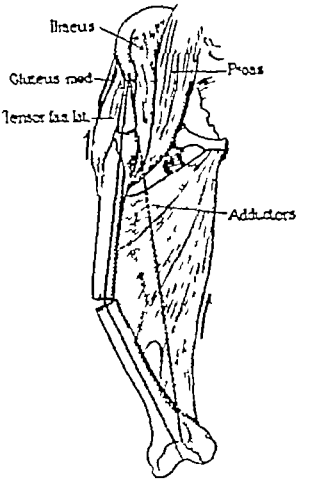

Fig 14 Diagram of muscle pull applied to fracture about the middle of the femoral shaft, demonstrating the displacing effect of adductors on the lower fragment.

their activity, their nerve supply, their viability It is only by this conception that one visualizes a fractured femur at the junction of the upper and middle third, with the upper fragment being externally rotated by the powerful external rotator muscles and flexed by the ileopsoas (Fig 13, femur), a fragment too short to be controlled by any means other than operative fixation Then one realizes there is a long lower fragment that can be controlled by traction, suspension, and rotation, and that the tension of the obliquely pulling adductors can be relieved of the spasm created by the irritation at the point of fracture if there is careful balancing of traction against their displacing effect (Fig 14) This great adductor group can be prevented from producing an angulation at the point of fracture if the limb is properly suspended and weight applied sufficient to overcome its pull One will also see immediately that it frequently is impossible to control a fracture of both bones of the forearm occurring between the supinators and pronators, because of the great angulating pull of these muscles, and will resort to open operation before there is fibrosis, tissue, or callus around the site of fracture and contracture in the muscles attached to the fractured bones, which almost precludes even the operative replacement and retention in anatomical alinement and rotation He will know that a fracture of the surgical neck of the humerus, put up in full abduction, has such a tremendous pull placed on the upper end of the lower fragment by the pectoralis major, that it cannot be held by anything other than lateral traction, which it is impossible to apply because of the brachial nerves and arteries that lie immediately between the skin and the medial surface of the bone (Fig 15, shoulder) If these and many other principles were understood and were borne in mind when any fracture is being treated, there would not be so many difficulties and so many bad results

I quote from an article written by Dr George Crile, which appeared in the *Annals of Surgery* in October 1919, after his experience with many war injuries He entitled it "The Good Surgeon"

The surgeon and the pathologists who for four years have intensively studied war wounds have formulated many theories of treatment—many apparently contradictory theories Thus there have been presented the claims of the value of various chemical agents against those of no chemical agent, of moist dressings against dry, of heat against cold, of frequent dressings against infrequent dressings, and of no dressings against both, of sunlight and of

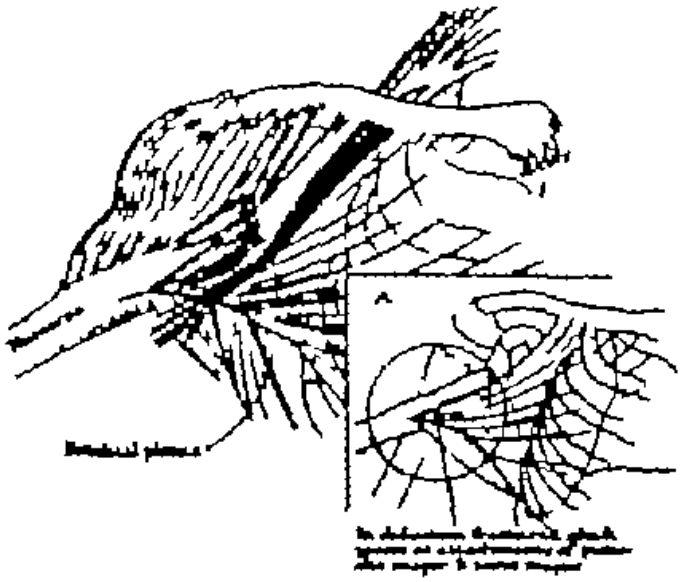

Fig. 15. Fracture at the surgical neck of the humerus, demonstrating the action of the adductor muscles of the humerus becoming a fulcrum which causes the upper end of the lower fragment to descend as the lower end of the same fragment is brought into abduction. This involves not only displacement of the upper end of the lower fragment but may injure the brachial plexus by angulating it over the sharp edge of this fragment

electric light against occlusions of immersion against hot air of bacteriological control against clinical judgment of vaccine toxin and foreign proteins against normal reaction of wound inoculation with harmless organisms against wound sterilization of isotonic against hypertonic solutions paste has competed with paste bipp with ip, sap with both, and chromic paste with all

Does not this intensive study of infection in war wounds for this comparatively short period equal and recapitulate the more leisurely study of infection during the 30 years since Lister first proposed the carbolic spray? And is there not slowly emerging from the present conflict of opinions the same fact as that which emerged from the post Listerian period—that the one agent of successful surgery whether war surgery or civil surgery *is the good surgeon?*

We cannot hope that all surgeons who treat fractures are good surgeons in every line, and the definition of a good surgeon is very broad The surgeon, however who attempts to treat fractures should consider first whether he is the type of surgeon to treat the fracture confronting him. Has he the fundamental knowledge and the mechanical skill to meet the exigencies of the case? His conscience must be his guide and if his conscience misleads him to attempt something that results in a crippling deformity which could have been prevented he will have erected a monument that probably some day he will wish to hide and will have made somebody's life a burden that could have been a pleasure. There are no splints which reduce fractures automatically

Looking back 25 centuries to Greece, we find the same principles described in the treatment of fractures that we use today or should use. Civilization has progressed in some ways, but the anatomy and the temperaments of people have not changed. We have at our command X ray equipment and mechanical appliances that the ancients did not have. We also have many types of fractures, due to the speed of the times both in industry and in transportation, which they seldom, if ever met. But if we use our knowledge of anatomy and physiology and build up fracture treatment on the basis of this knowledge using the X-ray operative surgery and the approved mechanical devices, there is no reason why there should be as many poor results in the treatment of fractures as there are today

Hippocrates teaching is still the best teaching A fracture should not be allowed to go to the second or third day but should be reduced, and properly reduced, as soon after it occurs as it is possible to apply the reduction apparatus, which is thought out to meet the needs of that particular case—whatever they may be. Let us forget any particular method and when we see a fracture, look through the skin to the tissues that lie underneath weigh the value of any method for that particular fracture or invent a new one and reduce it once and for all so that it will stay reduced. Principles stand from generation to generation gadgets come and go. Let us go and sin no more!

ADRENAL CORTICAL TUMORS[1]

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CORTICAL adrenal tumors have produced marked changes in physical characteristics and in metabolism Some changes which resemble these have been described as caused by certain tumors of the pituitary (13), the pineal gland (58) and the ovary (7) A study of adrenal cortical tumors with the metabolic and secondary sex changes is presented

Tumors arising from the suprarenal gland can be classified as (a) those arising from the various layers of connective tissue, or from blood vessels, lymphatics, or nerve structures within the gland, (b) those arising from the medullary cells, and (c) those arising from the cortical cells

Of the tumors occurring in group A, those recorded are fibroma, neurofibroma, myoma, osteoma, lipoma, hemangioma, lymphangioma, and melanoma Goldzieher has classified the types arising from the medullary cells on the basis of embryology, into tumors from the sympathogone, sympathoblast or pheochromoblast cells, and those tumors from the sympathetic ganglion, or ganglioneuromas, and those from the pheochromocytes, or paraganglioma Ewing has classified cortical tumors as hyperplasias, adenomas, and carcinomas

Hyperplasias, or well defined nodules of cortical cells, have been reported as common Goldzieher states that nodules are to be found in 33 per cent of all adults and that it is difficult to distinguish between nodular hyperplasia and small adenoma Nodular hyperplasia has been suggested as being a regenerative process following infectious damage to the adrenal gland

Adenomas vary in size from a pea to a goose egg or larger, are frequently bilateral, usually globular, and set off from the remaining adrenal tissue They may be definitely encapsulated The color is a sulphur yellow and often may be mottled with dark, pigmented brown or red areas Microscopically the cells are those of the adrenal cortex. They may simulate those of the entire cortex, including pigment of the reticularis In large adenoma, Goldzieher states that the structure may resemble the zona fasciculata In cases with symptoms of hirsutism, Brostner and Vines state that they have found a deep fuchsinophil staining power in the cytoplasmic granules of the reticularis Confirmation of this finding has been published by Goldzieher and Koster who state that the reticular layer is also widened There is usually an abundance of lipoids Lubarsch states that glycogen is scarce in these adenomas The proliferation of the stroma may bring about a deceptive picture of the papillary growth but Prym states that real tubular or papillary structures are not formed—a feature which distinguishes these adenomas from the so called hypernephromas of the kidney

Geschickter reports that most of the adenomas are asymptomatic and are found accidentally at autopsy In his study of 72 adrenal tumors, 63 were so discovered He states that the distinguishing characteristics of cortical adenoma are definite cortical cells, tendency to lipoid degeneration, marked capillary network, pigment deposits, and the arrangement of the cells in cords and bundles

Neoplasms of the cortex proper and neoplastic tumors developing from accessory "interrenals" are not common Tumors arising from adrenal rests occur in various parts of the body in the kidney, the liver, the pancreas, the retroperitoneal tissues, and in the testis and broad ligament True renal tumors which resemble the adrenal cortex are considered by most to have nothing to do with the adrenals The difference in these tumors has been well brought out by Ewing In a real adrenal tumor, there is a loose relation of the cells to one another and to the stroma Areas of diffuse growth, or indifferent

[1]Presented before the Clinical Congress of the American College of Surgeons, San Francisco, October 28–November 1, 1935

spheroid cells, or spindle cells are practically unknown in renal tumors but are frequent in adrenal growths. Giant cells form in both varieties of tumors perhaps to a greater extent in those of adrenal origin. Fraser states that the primary structure of the two tumor types is decidedly different, and that only secondary structures due to malignant change or degeneration can cause the renal to resemble adrenal growths.

Hypernephromas of themselves are thought *to occur rarely in the adrenal. Ellis has* estimated them at less than 2 per cent. According to Goldzieher in the cells of adrenal origin the cytoplasm is foamy granular and interspersed with lipoid granules. In renal tumors the cells are remarkably clear throughout, resemble vegetable cells, and contain large globules or crystals of fat with hydropic fluid and little or no granular material. Hydropic vacuolation and an abundance of *glycogen are two noteworthy features of renal* carcinoma. Both are absent in the adrenal cell type, the glycogen content of which is usually negligible

Tumors arising from the adrenal cortex proper are usually soft growths of a yellowish color with a tendency to hemorrhagic areas, and at times with areas of necrosis They may vary in consistency being more solid in some parts occasionally may develop cystic areas following necrosis at first are definitely encapsulated but later may grow through the capsule and invade other tissues They are most commonly reported as invading the kidney which occurred once in our series (Case 5) The tumor may invade the kidney pelvis and the renal vein with thrombosis of the vena cava When metastases occur they are most frequently seen in the liver and lungs *Bone metastases, common in renal tumors,* seem to be rare in adrenal tumors. Harris and Pflews, in reviewing the literature reported that in 15 cases at autopsy metastases were found in the liver 5 times, the lungs 3 times, and the liver and lungs *combined* twice. Stevens, in an analysis of 74 cases from the literature found metastatic reports as follows liver 27 kidneys 16 lungs, 14 skull 11 (possibly some orbital skull metastases from medullary tumors of Hutchinsonian type) the opposite adrenal 9 the peritoneum, 7 the brain 5 the lymph glands—aortic, bronchial and mesenteric, 14 the pancreas, heart, mediastinum, and ribs, 3 the spleen and intestines 2 and the ovaries, 1

Microscopically cortical adrenal tumors, at times, may resemble the zona fasciculata This was apparent in our Case 1 without endocrine symptoms. In the cases with endocrine symptoms, the cells bear greater resemblance to those of the zona reticularis *This was reported by Brostner and Vines* in their cases of hirsutism similar findings were reported by Goldzieher and Koster but not in definite tumor cases. In our Case 1 in 1930, this difference was noted in contrast to our Case 2 with endocrine change.

The adrenal is frequently involved in metastases, secondarily to other organs. Burke, in analyzing autopsy records of 371 cases with malignant tumors, found the adrenals involved *in 49, only 2 of which were* primary in the adrenals.

SYMPTOMS

Cortical adrenal tumors may be asymptomatic or symptomatic symptoms varying according to sex, age, and the degree of malignancy *Definite adrenal cortical tumors* are reported without any apparent endocrine changes and with only the presence of the tumor and symptoms of malaise accompanying it.

Langeron and Loheac classify the various symptoms of adrenal cortical tumors as follows (a) tumors with endocrine symptoms (b) tumors with only an abdominal mass; (c) tumors with metastatic masses (d) tumors with arterial hypertension, either paroxysmal or continuous.

When adrenal cortical tumor occurs in the male before puberty there is frequently an increase in muscular development, the so called Herculean type. Harris and Pflews report this occurrence in 60 per cent of the male children in their collected cases. With the muscular development a marked growth of hair occurs on the face, body extremities, and genitals. Rapid growth may take place early but is later replaced by ossification of the bones and absorption of the epiphyseal

cartilages When the disease occurs before birth, closure of the cranial sutures has been reported The dentition is rapid, and 1 case is reported in which dentition was almost complete at 6 months of age The muscular development is frequently accompanied by marked athletic ability, out of proportion to the age of the individual The growth of hair is usually dark, coarse, and at times so thick that the genital area resembles the ape more than the human, so completely is the skin hidden There is a change in the skin in that it is more dry than normal, and the acne manifestations, so frequently seen at puberty, appear on the face and chest Some cases develop duskiness of the skin of the face and hands The external genitals increase to adult size, and premature puberty as well as paternity has been claimed The picture is mainly one of premature maturity Precocious tastes develop, as the fondness for smoking cigars seen in our Case 6, of prepuberty virilism which, however, was not proved to be a tumor of the adrenal Premature senility has been reported in slow growing tumors Precocious mental development has been reported in 5 cases with marked dullness in 2 (Harris and Pflews)

It has been stated that in the male after puberty, no further change toward masculinity is possible In support of this, Hartman reported a case in which the symptoms were pain in the abdomen and chest with marked weakness, and with a mass in the right side of the abdomen, which on transperitoneal removal proved to be a malignancy of the adrenal cortex Stevens reported a similar case following injury Gibson reported a case with operation for tumor of the cecum with possible liver metastases, which on autopsy proved to be a right adrenal hypernephroma From the autopsy records of Presbyterian Hospital, the history of Case 5 was obtained This case presented shortness of breath, weakness and cough, with evidence of consolidation of his right chest Aspiration of the patient's chest showed tumor cells, epithelial in type Autopsy proved he had a carcinoma of the right adrenal cortex with metastases Tremoliers reported a man of 25 years with symptoms of fatigue, fever, and sepsis, who died in cardiac collapse and who on autopsy, showed cortical malignancy of both adrenals

In contradistinction to these cases of cortical adrenal tumors is the one reported by Macera in which the patient developed adiposity, an increase of hair over the normal, very large genitals, and suffered from polydipsia Autopsy revealed cortical carcinoma of the adrenal with pulmonary metastases An additional case with endocrine change was reported by Long and Gray of an acromegalic man of 45 years with pain in his hands and feet, edema and pigmentation of the hands and feet, and with bone metastatic tumors on X-ray examination Autopsy showed a large right cortical adrenal malignancy, a very small left adrenal, generalized metastases of the tumor, and an overgrowth of the pituitary by atypical epithelium with no resemblance to the adrenal tumor cells Weber, in addition, cited 2 cases from the literature in which endocrine changes occurred but not towards the adult male type. One was a case of Dr J D Zum Bush a young man aged 27 years had an enlargement of both mammæ with secretion, and on autopsy, a hypernephroma of the left adrenal cortex was found with multiple metastases The other was a case of Bittorf-Matthias a man of 26 years had dyspnea, hypertrophy of the mammæ and atrophy of the testicles Later a tumor developed in the left side of the abdomen which, on autopsy, proved to be a hypernephroma of the adrenal cortex

From these citations, if the observations are correct, the male after puberty may show some endocrine imbalance such as adiposity and increase of hair At times, he may show the pigmentation and weakness associated with Addison's disease when both adrenals, or a solitary functioning adrenal has been affected At times he may show similar changes with sepsis, if necrosis of the adrenal occurs Rarely, he may present changes in the mammary glands (gynecomastia) similar to changes in chorioepithelioma of testicular teratomas However, the usual symptoms appear to be weakness associated with the malignancy and the presentation of the tumor in the abdomen

In the female, when the disease occurs before birth or in early infancy, the symptoms

have been described as pseudohermaphroditism. Gallais, in his study of 67 cases presenting suprarenal lesions in the female, divided the cases into 4 types (a) pseudohermaphroditism, (b) virilism suprarenal, (c) form menstrual, and (d) form obstetrical. He stated that in the pseudohermaphrodite, the virilism is developed to the highest degree. It appears in the genital organs giving the illusion of the male sex, with the sex characteristics clearly masculine. If it occurs in embryonic life, the result is hermaphroditism. Cecil cites Crecchio's case of an individual who was baptized as a girl but brought up as a boy and who apparently was masculine in sex until he died at 40 years of age. On autopsy a uterus, tubes, and small ovaries were found with extreme hypertrophy of the adrenals. Cecil states

> Such changes taking place after birth have led to the belief that congenital pseudohermaphroditism in the female is due to abnormal hypersecretion of the cortex during embryonic life. All degrees of such anomalies are found from only slight enlargement of the clitoris to enormous enlargement of the clitoris, accompanied by atresia or total absence of the vagina. The internal genital organs are usually small and sometimes greatly deformed. Such deformities do not increase, nor is there a change toward the normal. It would seem that if such defects were the result of hypersecretion of the suprarenal cortex, it was rather early in embryonic life and that later the suprarenal would cease to exercise such abnormal control. With the exception of cortical tumors, I have seen no report of abnormalities of the suprarenals that might have been responsible for the condition. Removal of one suprarenal has failed to have any beneficial effect.

An additional review has disclosed no cases of pseudohermaphroditism in the literature that had changes in the adrenal except that of tumor

In the female highly malignant tumors occurring before puberty cause death before marked changes occur This, however is not a common occurrence and most cases seen have the characteristic syndrome toward masculinity Obesity is frequently associated with the change. This change to obesity from slight to very stout, with the fat on the face and trunk, was described by Fox, Ogle Bullock and Sequiera, Richards, Glynn and others. Muscular hypertrophy has been observed by Sézary and Loman, and Jump, Bates and Babcock, but it is not frequent. There is a growth of hair on the genitals followed by growth on the face, body and extremities. The mammary glands are reported to have increased in size. The skin becomes red, coarse, dry and the acne of puberty frequently occurs. The voice becomes deep, often cracks, and the vocal cords on examination are reported as increased in size. Ossification of the epiphyses is frequently observed. The appearance is reported as sullen. Most of the children have been mentioned as bright but Harris and Pflews stated that the frequency of bright to dull was 5 to 2 The changes in the sexual organs vary from slight to marked. The clitoris increases in size and in appearance resembles a penis. The labia enlarge, especially the labia majora, and are deep red. The entire genital region, pubis, and thighs are frequently covered with thick, dark and long hair As a rule, these patients do not menstruate even though the age of puberty has been reached. To this there are two possible exceptions one a case reported by Bullock and Sequiera of a girl whose menses began at 10 years and second, a case cited by Cecil, the menses beginning when patient was 2 years old. Harris and Pflews have reported a fall as the traumatism that injured the adrenal in a child and which was followed by an adrenal tumor with symptoms

In the female after puberty and before the menopause, the changes vary according to the rapidity of the progress of the disease. The first symptoms are usually scantiness of menstruation, followed by cessation. Frequently headaches occur at the time when menstruation should have occurred. When the menses cease, the cessation is complete. Associated with the absence of menstruation, there is a complete loss of sexual desire and an absence of libido In some, there is the loss of normal feminine modesty in others it is unchanged. Attraction to the same sex is reported by Holmes with a recurrence back to normal attraction to the opposite sex after removal of the tumor In none of our cases was there any change in sex desire of a homosexual type On close questioning there appeared to be a complete absence of sex

thoughts in the adults but the young woman (Case 3) was still attracted to the opposite sex The menses returned after the tumor was removed The return of sex attraction and libido occurred after resumption of the menses If metastases occurred later, the menses ceased with the regrowth of the tumor (Case 2) Shortly afterward or coincident with the cessation of the menses, there is a marked increase of growth of hair, called hirsutism by Apert The hair begins to grow on the face and the pubic hair changes from the feminine outline to the masculine The hair on the face and body is uniformly dark, very coarse and long The hair on the head becomes coarser and dry One of our patients (Case 4) a woman of 36 years of age, began to become bald on the top of her head, resembling her male parent at a similar age Hair may appear on the shoulders Its distribution is frequently more marked than it is in the male. In one of our cases a girl of 16 (Case 5) the hair was so profuse on the thighs abdomen pubis and anal region, that the skin could hardly be discerned through the mass of hair As a rule daily shaving removes the hair from the face When the tumor is removed the hair falls out and the feminine pubic line is reestablished The loss of hair is most pronounced at the menstrual periods and the depilation is most marked while bathing Replacement of the hair of the head with the type of hair previous to the onset of the tumor is reported

The skin changes becoming dry and coarse A red face occurs frequently Duskiness and redness of the face and hands is reported somewhat similar to that described by Cushing in basophilic adenoma of the pituitary Acne of the face chest, and shoulders occur Pigmentation of the skin is reported by Lineblatt and, in a male by Long and Gray Striæ atrophicæ are observed on the abdomen and thighs, and in females who have previously borne children, those present become more marked

Obesity occurs apparently more often with the less malignant tumors The fat is more restricted to the trunk and the face and neck somewhat similar to the description in Cushing's syndromes In more malignant tumors, the fat is later replaced by angulation and emaciation

The voice becomes deeper and somewhat masculine In young women it frequently "cracks" like a boy's at puberty The vocal cords have been reported to have increased in size After removal of the tumor the voice slowly returns to normal Some cases show a rapid change especially as shown in our Case 3, where a phonographic record before operation was the index

There are changes in the secondary sex organs but they occur more slowly than those of the menses and hair In females still in the growth period, the clitoris greatly enlarges and may assume the appearance of a penis In our Case 3, it had the power of erection to about 2½ inches and when so erect was strikingly like a boy's organ The labia enlarge, especially the labia majora and assume a dark color The vagina has not been reported as changed The uterus has been reported as both normal and small In most cases at operation the ovaries have been described as small and atrophic On vaginal or rectal examination there is loss of the usual ovarian sensitiveness After a successful removal of the tumor the clitoris slowly diminishes in size and the uterus if small, may resume its normal size on resumption of the menses The ovaries have been described as increasing in size upon palpation with return of the menses and with a return of normal sensitivity

In the young females there is no normal development of the breasts but they resemble those of boys In adult females there may be a reduction in the size of the breasts but after operation and cure they return to their normal size

Some patients develop masculinity in their muscular changes The increase in muscular tone and strength gives them an athletic superiority as was so marked in our Case 3

Changes in the mental states of these patients have been reported by Gallais Patients may become emotional Murray and Simpson reported that their patient was irritable and depressed as in our Cases 2 and 4 However, in 2 of the females in our series who had previously borne children, there was no

apparent diminishment of the normal maternal love and care.

Edemas of the face, feet, and hands have frequently been reported especially in cases of rapidly growing tumors. Headaches, especially at the expected time of menses are of frequent occurrence. Weakness and palpitation of the heart have been reported at the same time. Shortness of breath was a frequent complaint.

Symptoms referable to hypertension are frequent. If hypertension does occur it is apt to be continuous and not of the paroxysmal type as reported with medullary adrenal tumors.

Insomnia was the complaint in a case reported by Anderson. Epileptiform attacks occurred in a case reported by Meyer and Trumess. However the patient died before a diagnosis could be made. This is not an uncommon terminal symptom of acute cortical adrenal failure.

In females past the menopause the symptoms naturally have no change in the menses. Increase in hair and obesity have been reported but no change in the secondary sex organs was noted. A case has been reported by Goldschwend in which emaciation in contrast to obesity was the outstanding symptom with hirsutism. In these cases there seems to be an entire loss of superficial fat, and it has been suggested by Cecil that the emaciation was produced by the destruction of the adrenal tissues.

An interesting phenomenon has been reported, called the Achard-Thiers type, in which associated with adrenal cortical tumor are symptoms of obesity hypertrichosis, and diabetes. The various causes of the metabolic disturbances have not been established but so far have been attributed to a plurigland ular disturbance and not entirely to the adrenal tumor.

DIAGNOSIS

In cases without endocrine symptoms the tumor as a rule, has been large enough to be palpable in the abdomen in the region of the kidney. Not infrequently this type produces pain. These tumors displace the kidney downward. The displacement has been demonstrated by X ray and particularly by pyelograms. In the displacement the upper pole is frequently pushed downward and inward with the hilum of the kidney facing downward. This is the reverse of the usual picture of a nephroptotic kidney and does not resemble the congenital, unascended kidneys in which the kidney usually unrotated has the hilum facing anteriorly. In some cases, invasion of the kidney has been demonstrated by irregular compression changes in the pyelographic shadows in the upper pole. These cases have been difficult to differentiate by pyelograms from tumors of the upper pole of the kidney.

When the characteristic syndrome of "genito-suprarenalism" is present the diagnosis lies between tumor of the adrenal hyperplasia of the adrenal, and possibly basophilic adenoma of the pituitary. Ovarian tumors, as arrhenoblastomas, are reported to have produced symptoms that might be confused with adrenal cortical tumor.

Hirsutism occurs in pituitary ovarian, and adrenal tumors. Goldzieher and Koster state that of pituitary origin is usually silky lanugo-like, and facial growth predominates on the cheeks that due to abnormal ovarian function is universal and of typical masculine character that due to adrenal cortical activity is characterized by coarse, dark hair on the chin and upper lip besides wide distribution all over the body.

The obesity of these glandular disturbances has some slight difference in the various types. The pituitary has been characterized as the girdle type of adiposity the ovarian as generalized, and the adrenal as involving the body and not the extremities.

Tumors and enlargements of the adrenal have been diagnosed by X ray either through the density of the tumor shadow itself, or through the tumor displacing some shadow-forming organ, usually the kidney. Carelli in 1921 demonstrated that carbon dioxide infiltrated into the perirenal fascial planes would be of value in visualization of the kidney kidney capsule, and adrenal. Langeron, in 1929, showed that intraperitoneal air would enable one to visualize an adrenal tumor by X ray. Roux Berger Naullean, and Coadiates, in 1932 diagnosed a cortical adrenal tumor by aortographic X-ray using the method of Reynaldo dos Santos. They in-

jected 40 cubic centimeters of thorotrast into the aorta through the left lumbar route and brought about visualization of the arterial supply of the kidney, the tumor, and the spleen upon X-ray

Since 1930 we have used the method of Carelli, modified as described in a previous article (8) This method has been of value in demonstrating both pathological and normal adrenals The air injected into the perirenal fascial space was displaced by manual pressure around the adrenal areas, and then upon X-ray the air was shown infiltrating around the adrenal and upper pole of the kidney It is possible to outline the adrenals and with the change in size, shape, and position of the adrenal shadows, to have a tenable diagnosis of tumor, and it is possible to determine whether or not there is the presence of a shadow of an apparently normal adrenal on the opposite side Photographs of the negatives and tracings of the same are shown

Of additional interest in the diagnosis have been the studies of hormones in the urine of patients with genitosuprarenal syndrome In our Case 2, Kurzrok in 1930 found no prolan A in the urine but was able to demonstrate the presence of considerable quantities of a follicular hormone Apparently this was the first time that this observation had been made The first report of this finding was made by Frank in 1934 in 2 cases of adrenal cortical tumors confirmed by autopsy In these cases, large amounts of female sex hormone up to 57,000 mouse units were found, with tests negative to pregnancy, and with no increase in the pituitary sex hormone Later confirmation of these findings was observed in our Case 3, in which the follicle—stimulating hormone was negative, but the follicular hormone showed 8 rat units per liter In one other of our patients (Case 9), with hirsutism but with no diagnosable tumor by air injection X-rays, a similar finding of 8 rat units per liter of follicular hormone was observed In still another patient (Case 7), in which the differential diagnosis rested between a basophilic adenoma of the pituitary and adrenal change, and a normal sella turcica by X-ray and with bilateral enlargement of the adrenals by air injection X-rays, the follicular hormone varied from 3 to 8 rat units per liter Of great interest also is the case of the boy (Case 6) with marked sexual precocity and hirsutism in which various amounts of a hormone (theelin) were found

There is the possibility that these various tests may offer a help in the diagnosis of some of the syndromes in adrenal tumors, as suggested by Frank Further observations will be necessary to determine their values in endocrine disorders and they may be of significance in tumors The occurrence of these hormones in the urine in large amounts, in males as well as females past menopause should be, from the above observations, suspicious of adrenal cortical change

It is interesting to note the prompt disappearance (5 days) of the follicular hormone from the urine shortly after the removal of the tumor (Case 2) It is to be regretted, however, that her symptoms recurred in 9 months with demonstrable pulmonary metastases, but no determination of the hormones in the urine was made

Sugar tolerance tests have been suggested as an aid in the diagnosis of adrenal tumors but our experience reveals only 1 case with a lowering from the normal (Case 2) It is possible that in this case there might have been other factors governing this, apart from the adrenal cortical disease No autopsy was obtained and the condition of the pancreas was not determined

OPERATIVE TECHNIQUE

Three different routes of approach have been used for removal of the adrenals (1) extraperitoneally, through the lumbar region, (2) transthoracic route, and (3) transperitoneal route

The lumbar route with an extraperitoneal approach has been used extensively in adrenal operations by Crile It has been used for removal of tumors by Mursell, Jump, Bates and Babcock, Kennedy and Lister, Murray and Simpson, Crosbie and Smith, Walters, Wilder and Keplar, and for hyperplasias by Goldzieher and Koster, and others Walters, Wilder, and Keplar have done bilateral exposures of the adrenals to determine, first, the diseased side and, second, to be satisfied that

there was an opposite adrenal present. A similar procedure was used by Goldrieher and Koster in their obesity cases.

The transthoracic route has been used by Broster and Vines in most of their cases of adrenal genital syndrome. This they claim is the easiest approach in view of the fact that the adrenal vascular pedicle allows a slight range of upward movement. It has the disadvantage of creating an artificial pneumothorax. They also attempted a subdiaphragmatic route by fracturing the last rib at its neck and retracting this up with the diaphragm. This exposure they state, is not so satisfactory Inaccessibility deep bleeding, delicate traction on a friable organ through what may be a spasmodically movable and confined space, are the main difficulties of this route. In the transthoracic approach it was first necessary to do a preliminary laparotomy for exploration of both adrenals by palpation, and then after recovery perform the main operation by the transthoracic approach.

In an approach to an adrenal with tumor the ideal method should be ligation of the adrenal vessels, particularly the veins, before any manipulation of the tumor With the tumor the adjacent fascia containing the lymph vessels and nodes should be removed. As this requires an adequate exposure especially if the tumor is large, we think it is best done transperitoneally

In the past we have removed medullary tumors through the lumber route with ease and also with great difficulty but since we have removed the cortical tumors transperitoneally through the oblique, subcostal incision the safety of the operation, its ease of performance, and the completeness of removal that is possible of attainment by this approach, commends itself as the most satisfactory In addition it is possible, by palpation of the opposite adrenal, to corroborate the findings of the air injection X-rays concerning the presence of an opposing adrenal In fat subjects the information derived from palpation is often uncertain and the palpation of a mass combined with a shadow by X ray are both only suggestive evidence of a functioning adrenal We have used the vertical rectus incision on both sides as well as the oblique subcostal and feel that the latter gives a better exposure

The oblique incision began at the ensiform and extended along the costal flare until adequate exposure was obtained depending on the obesity of the patient. The exposure was facilitated by use of an elevated bridge on the table, situated so that the costal flare is opened and the subcostal area projected forward as often used in common bile duct exposure. The posterior parietal peritoneum was opened to the right of the duodenum and across and above the colon On deflection this exposed the adrenal and renal area.

The right adrenal presents more difficulty than the left because it enlarges to a considerable degree around the vena cava and its central vein is short and empties directly into the cava (Fig 13) The vessels were first ligated and divided, and then the tumor was delivered with its fascia. The ligation of the veins on the left side was much easier because the central vein empties into the left renal vein (Fig. 14) and is directly accessible

Manipulation of the tumor before the ligation of the vessels was avoided first, to prevent possible metastases from that cause, and second to prevent the possibility of large amounts of adrenal secretion being injected into the circulation To this has been attributed the collapse that sometimes occurs immediately following the operation. Such collapse appeared to be a reaction similar to the injection of large doses of epinephrine. The retroperitoneal approach to the left adrenal was just above the colon, and care was taken not to injure the splenic vessels lying between the adrenal and the tail of the pancreas

Transperitoneal adrenalectomy for tumors has been successfully used by Hartman Collett, Neligan, Holmes, etc.

Cecil states that following removal of the tumor it has been found in the literature that 30 per cent of the patients are reported to have died soon afterward of shock. Of the patients who have recovered he states it has been reported that 66 per cent had severe shock In our cases, 2 had a similar picture which was ascribed to adrenal failure In 1 the failure was temporary and she recovered (Case 2) and the other died (Case 4) With this state

of shock there was marked elevation of temperature but the patient was rational and felt comfortable The pulse was small and very rapid—over 160 The blood pressures were very low 55/45 to 68/48 In Case 2, the administration of large amounts of saline with ephedrine and daily transfusions for 2 days, brought about recovery The improvements noted immediately after the transfusions, we thought, were possibly due to the hormone in the normal blood The recovery after 48 hours was thought to be due to one of two causes either the shock was from excessive adrenal secretion introduced into the blood at the time of operation, or the remaining adrenal was in a state of suspended activity and there was a deficiency period of adrenal hormone until the other adrenal began to function From the time element and from animal experimentation, the latter would appear to be more probable

In the fatal case, large doses of sodium chloride solutions were given according to investigations by Loeb, with transfusions and eschatin (a cortical adrenal extract) The collapse continued and the patient died in convulsions resembling those of adrenalectomized animals This case was especially interesting because by air injection X-ray the patient's apparently normal adrenal was the smallest adrenal visualized in any of our air injection cases Cases have been reported in which the recovery has been facilitated by cortin (Prather) However, if there is no remaining adrenal tissue, very large doses would be necessary to have any effect according to the experiments on animals In about 30 per cent of the reported cases the opposite adrenal was either absent or inadequate to support life In the other patients operated upon in this series, large amounts of saline and transfusions were administered although there was no evidence of collapse

X-ray therapy has been reported by Apert and Bubost to have produced favorable results when applied to the tumor area in patients not operated upon We saw no beneficial results from the X-ray therapy to the metastases in the lungs in Case 2 It is possible, since the adrenal cortex arises from the same anlage as the testis, that future investigation may prove that some of these tumors may be susceptible to the X-ray as are some of the testicular neoplasms

CASE REPORTS

Here is a study of 10 cases The first 5 cases had proved adrenal cortical tumors, the second 5 had symptoms suggestive or characteristic of the disease, but there was no demonstrable evidence of tumor

CASE 1 Chart 69341 A S, a single woman, Canadian, of Scotch ancestry, was admitted July 21, 1927, complaining of intestinal trouble Her father had carcinoma of the lip and her mother had high blood pressure Patient was the youngest of 6 normal children and had had the usual childhood diseases Her menses began at 14 and were regular For the last 8 to 9 months her menses were scanty and she missed the last period Her present illness began in 1926 with severe right sided pain radiating across her abdomen, and with fever She developed tenderness near the umbilicus She was treated medically and made improvement A second attack occurred in April, 1927 Her distress had become more marked and she felt a tender mass in the left upper abdomen She had nausea and vomiting and a slight cough She had noticed a slight increase of hair on her face and arms She was thin, active, nervous, intelligent Her abdomen had a large firm mass in the left upper quadrant and flank. Cystoscopy showed a normal bladder, normal ureters and normal functioning kidneys Pyelograms showed a normal right kidney but a low left kidney with a dense mass above Her chest and diaphragm were normal by X-ray Blood count was practically normal, as was her blood chemistry Blood pressure was 155/68 Wassermann was negative

Operation was performed July 29, 1927, and a left upper rectus incision was made The peritoneum was opened and explored A large, round mass, covered with dilated veins, and the size of a very large cocoanut was in the left upper lumbar gutter It was retroperitoneal, below the spleen and free from it The mass carried the colon downward and outward on its anterior surface, and was separate from the kidney which it has apparently pushed downward. The posterior peritoneum was cut external to the colon around the splenic flexure, the colon was peeled off the tumor from without and above, down inward, mobilizing the colon The inner border of the mass was freed and a large vascular pedicle of the tumor was exposed This was just above the vascular pedicle of the left kidney The pedicle was ligated and the tumor was freed, and removed from the lumbar gutter with surrounding areolar tissue It was outside the renal fatty capsule, was grooved at its posterior, inferior surface where the renal vessels passed The mass was not attached to the pancreas The colon was sutured back into place

The area from which the mass was removed was drained with a cigarette drain through the incision. The wound was then closed in layers.

The patient's condition was fair after operation. She was given hypodermoclysis of 1,000 cubic centimeters and a transfusion of whole blood, 500 cubic centimeters. *She made an excellent recovery.* Her wound healed well and she was discharged to return home on August 25, 1928. The patient improved at home until January when she had a recurrence of abdominal distress with loss of weight. An enlargement, nodular in character, was felt upon her liver. In February 1928, she was operated upon in Nova Scotia, and a section of a mass attached to her liver was removed. This specimen received at the laboratory was submitted to the same pathologist who pronounced the tumor similar to the preceding one. Word was received that she gradually became worse and died in May 1928.

Pathological report. (S P 36423 hist. 69341.) The specimen is a tumor mass said to have been removed from the region of the kidney. It measures 17 by 9 by 5 centimeters. It is nodular and apparently encapsulated. The nodules vary from 0.5 to 3 centimeters in diameter. On section the nodular pattern is maintained throughout the growth. The tissue is dense, pale, tough with softer yellowish areas scattered through it. These are apparently areas of degeneration. A few of these are hemorrhagic. Nothing resembling kidney or ureter can be found. While the yellowish areas have the color of suprarenal tissue, nothing having the differentiated architecture of the suprarenal gland, can be found.

Microscopic examination. The tumor varies considerably in its morphology in various parts. In some areas it is differentiated, reproducing cords of epithelial cells with an arrangement reminiscent in turn of the zona fasciculata, the zona reticularis, and occasionally the zona glomerulosa of the cortex of the suprarenal gland. With the Schardach R stain, the varying lipoid content of the different cells is easily apparent. In the differentiated areas, the individual cells tend to be polygonal with faintly acidophilic vacuolated cytoplasm, and centrally placed nuclei. The nuclear markings are clearly defined and occasional mitosis can be found, they average 1 to every 6 or 7 high power fields. The cell bodies are indistinct and often the cells appear confluent. The cell groups are supported by a delicate reticulum which passes out among them from the larger supporting fibrous strands, which in turn connect with the fibrous capsule. Although many vessels accompany these strands, they seldom contain red blood cells. Many areas of tumor tissue are necrotic.

Merging with the areas of partial differentiation are others in which there is little or no differentiation. The cells in these areas are either isolated or in small groups varying greatly in size and shape. Many are elongated, and both undersized and oversized cell forms appear, the latter often with several nuclei. Mitoses average only 1 to every 6 or 7 high power fields. In both areas there is a tendency for the tumor cell masses to infiltrate the capsule and septa. No areas resembling true hypernephroma can be found. Fontana's stain shows no melanin. Laidlaw's silver reticulin stain shows that the tumor cells are silver positive and they do not form reticulum. There is no iron-containing pigment nor are there any nerve fibers.

Diagnosis: carcinoma of the suprarenal gland (*cortical type*).

Case 2 (Chart 249169) L.T., 36 years old, married, born in Russia, was admitted April 1, 1929. She complained of headache, weakness, palpitation, and cessation of menses for 2½ years. She particularly complained of an excessive growth of black hair all over the body.

The family history was negative. She had had a normal childhood. Her menses began at 16½ years, were irregular at first but after she was 18 were perfectly regular. She married at 22 years of age. During the war she had a nervous breakdown. Two children have been born, the first in 1920, the second in 1926. She has always been well. Her menses became scanty 2½ years before admission and then ceased. She developed severe headache at the time she would ordinarily menstruate, and she gained in weight. After a year, hair began to grow thick and long all over her body and she shaved frequently. Her face became reddened. The last 3 months prior to admission, she had shortness of breath and palpitation. For 9 to 10 months she had swelling of her ankles. There were no cyanosis, gastro intestinal, or urinary disturbances. Since cessation of the menses, she had complete absence of sexual desire, whereas before she had been quite normal.

On examination she was found to be a sturdy stout, extremely red faced woman, with dark, thick hair on her head and a dark straggly beard. There was slight puffiness of her eyelids. Her face had some acne marks. Her thyroid was not enlarged. She had a normal chest with full breasts. The skin of her chest, back, arms was covered with long black hair among which were numerous acne papules and scars. Her pulse was 130 to the minute. Her abdomen was obese and hairy with a male pubic hair distribution. After careful examination, a mass was felt deep in the right side. Her genitalia and legs were excessively hairy. The vaginal mucosa was cyanosed and the clitoris was larger than normal. Her cervix was soft and the uterus was larger and softer than normal. Her ovaries were not palpable and the fornices were less tender than usual. Her eye and muscular reflexes were normal as well as muscle tone and control. Basal metabolism was plus 51. Red blood corpuscle count was 5,300,000, hemoglobin, 124 per cent (Sahli), white blood corpuscles 15,000, platelets 300,000, polymorphonuclears 75 per cent, lymphocytes 15 per cent. Blood non-protein nitrogen was 41 milligrams per liter urea, 36 milligrams, creatinine, 1.8, and sugar 91 milligrams per liter. Wassermann was negative. Her eye grounds and perimeter test were normal. X-ray

examination of the osseous system revealed no abnormalities Cystoscopy showed a normal bladder and normal renal function Pyelograms showed the right kidney low with the hilum facing downward as if the kidney were pushed down Injection of air (300 cubic centimeters) into the perirenal space, followed by X-ray examination showed a large mass above the right kidney apparently pushing a normal sized kidney downward (Fig 2)

A glucose tolerance test on April 8 with 100 grams of glucose showed an increase of blood sugar per liter up to 20 0 from 88 in 1½ hours with an appearance of 4+ sugar in the urine The same day, the patient showed a blood cholesterol of 15 per cent lysin phosphorus of 7 1 and lecithin of 177 6 Bleeding time was 1¼ minutes, clotting time 45 seconds Fragility test was normal to controls Her oxygen capacity of 22 6 volumes showed a hemoglobin of 113 per cent

The Aschheim Zondek tests for pregnancy were negative on April 18 Urine tested on mice by Dr Kurzrok showed considerable quantities of ovarian hormone (follicular stimulating estrin)

X-ray film of the skull showed a normal sella turcica Her blood pressure varied from 105 105 to 160 110

Diagnosis of tumor of the right adrenal cortex was made and operation was performed on April 21 under gas-oxygen anesthesia An upper right rectus incision was made and the abdomen was explored The liver was very large and low the uterus was small and soft, and both ovaries were very small and firm There was a large retroperitoneal rounded mass above and separate from the right kidney, and directly above the right lobe of the liver The mass was firm and felt fixed The area of the left adrenal was palpated and sufficient tissue was felt but no evidence could be definitely obtained as to the adrenal The liver was lifted upward and the posterior parietal peritoneum was opened, the hepatic flexure and the duodenum being deflected inward and downward The tumor reddish in color was outside the renal fascia The tumor was removed without difficulty except where the venous pedicle apparently joined the vena cava near the liver notch Here the large size of the liver made visualization difficult However, the tumor was dissected off the vena cava and the large vein was ligated near the vena cava The artery to the tumor was cut off just above the renal artery from the aorta The tumor space was drained by a stab wound through the flank The peritoneal attachments were replaced and closed as was the anterior wound

Her condition immediately following operation was fair and she was given a clysis of 1,000 cubic centimeters of saline The next day she presented a peculiar condition of being apparently in good mental state, rational and with a feeling of well being, but with a fine thready pulse of 160 plus, a temperature of 103 degrees and a blood pressure of 55 45 on the left arm and 62 48 on the right arm She received 700 cubic centimeters of glucose and later

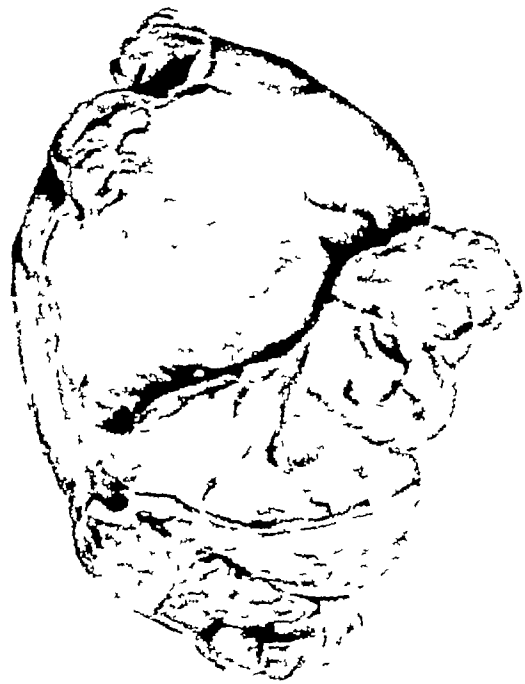

Fig 1 Case 2 Adrenal cortical carcinoma

600 cubic centimeters of whole blood Her pulse dropped to 140 and her blood pressure was 128 80 Her temperature that night was 105 degrees and her pulse 150 She was given 2,000 cubic centimeters of saline with 1 gram of ephedrine during the night Her hemoglobin was 75 red blood corpuscle count, 4 830,000 white blood corpuscle count 26,000—polymorphonuclear, 77, lymphocytes 17, eosinophils 1 myelocytes 4 The second day her blood chemistry showed urea 20 6 sugar, 154 cholesterol, 405 carbon dioxide, 51 3 Her blood pressure again dropped to 54 28 with a pulse of 165 She was given another transfusion of 500 cubic centimeters of whole blood Following this her blood pressure rose to 126 90 and her pulse went down to 130 The third day her hemoglobin was 75 per cent, red blood corpuscle count 4,500,000, white blood corpuscle count, 11,200—polymorphonuclear 80 per cent Blood chemistry showed urea 58 creatinine 3 76 uric acid 6 sugar 128 chlorides 405, and carbon dioxide, 49 1 She was given a clysis of 2 000 cubic centimeters of saline with 1 milligram of ephedrine Her blood pressure fluctuated between 164 98 and 154 90 She was rational and felt very well The fourth day her blood pressure remained between 145 80 and 160 100 Her chest was negative She felt well On the fifth day

The area from which the mass was removed was drained with a cigarette drain through the incision. The wound was then closed in layers

The patient's condition was fair after operation. She was given hypodermoclysis of 1,000 cubic centimeters and a transfusion of whole blood, 500 cubic centimeters. She made an excellent recovery Her wound healed well and she was discharged to return home on August 25 1928. The patient improved at home until January when she had a recurrence of abdominal distress with loss of weight. An enlargement, nodular in character was felt upon her liver In February 1928 she was operated upon in Nova Scotia, and a section of a mass attached to her liver was removed. This specimen received at the laboratory was submitted to the same pathologist who pronounced the tumor similar to the preceding one. Word was received that she gradually became worse and died in May 1928.

Pathological report. (S P 36423 hist 69341) The specimen is a tumor mass said to have been removed from the region of the kidney It measures 17 by 9 by 5 centimeters. It is nodular and apparently encapsulated. The nodules vary from 0.5 to 5 centimeters in diameter On section the nodular pattern is maintained throughout the growth The tissue is dense, pale tough with softer yellowish areas scattered through it. These are apparently areas of degeneration. A few of these are hemorrhagic. Nothing resembling kidney or ureter can be found. While the yellowish areas have the color of suprarenal tissue nothing having the differentiated architecture of the suprarenal gland, can be found.

Microscopic examination The tumor varies considerably in its morphology in various parts In some areas it is differentiated, reproducing cords of epithelial cells with an arrangement reminiscent in turn of the zona fasciculata, the zona reticularis, and occasionally the zona glomerulosa of the cortex of the suprarenal gland. With the Schultze R stain, the varying lipoid content of the different cells is easily apparent. In the differentiated areas, the individual cells tend to be polygonal with faintly acidophilic vacuolated cytoplasm, and centrally placed nuclei. The nuclear markings are clearly defined and occasional mitosis can be found, they average 1 to every 6 or 7 high power fields. The cell bodies are indistinct and often the cells appear confluent The cell groups are supported by a delicate reticulum which passes out among them from the larger supporting fibrous strands, which in turn connect with the fibrous capsule Although many vessels accompany these strands, they seldom contain red blood cells Many areas of tumor tissue are necrotic.

Merging with the areas of partial differentiation are others in which there is little or no differentiation The cells in these areas are either isolated or in small groups, varying greatly in size and shape. Many are elongated, and both undersized and oversized cell forms appear the latter often with several nuclei. Mitoses average only 1 to every 6 or 7 high power fields. In both areas there is a tendency for the tumor cell masses to infiltrate the capsule and septa. No areas resembling true hypernephroma can be found. Fontana's stain shows no melanin. Laidlaw's silver reticulin stain shows that the tumor cells are silver positive, and they do not form reticulin. There is no free containing pigment nor are there any nerve fibers.

Diagnosis carcinoma of the suprarenal gland (cortical type)

Case 2 (Chart 249169) L F 36 years old, married, born in Russia, was admitted April 1 1929. She complained of headache, weakness, palpitation, and cessation of menses for 1½ years. She particularly complained of an excessive growth of black hair all over the body

The family history was negative. She had had a normal childhood Her menses began at 16½ years, were irregular at first but after she was 18, were perfectly regular. She married at 22 years of age During the war she had a nervous breakdown Two children have been born, the first in 1920, the second in 1926. She has always been well. Her menses became scanty 2½ years before admission and then ceased. She developed severe headache at the time she would ordinarily menstruate, and she gained in weight. After a year, hair began to grow thick and long all over her body and she shaved frequently Her face became reddened The last 3 months prior to admission she had shortness of breath and palpitation. For 9 to 10 months she had swelling of her ankles. There were no cyanosis, gastro intestinal, or urinary disturbances. Since cessation of the menses, she had complete absence of sexual desire, whereas before she had been quite normal

On examination she was found to be a sturdy stout, extremely red faced woman, with dark, thick hair on her head and a dark straggly beard There was slight puffiness of her eyelids. Her face had some acne marks Her thyroid was not enlarged. She had a normal chest with full breasts. The skin of her chest, back, arms was covered with long, black hair among which were numerous acne papules and scars Her pulse was 120 to the minute. Her abdomen was obese and hairy with a male pubic hair distribution After careful examination, a mass was felt deep in the right side. Her genitalia and legs were extremely hairy The vaginal mucosa was cyanosed and the clitoris was larger than normal. Her cervix was soft and the uterus was larger and softer than normal. Her ovaries were not palpable and the fornices were less tender than usual Her eye and muscular reflexes were normal as well as muscle tone and control. Basal metabolism was plus 31 Red blood corpuscle count was 5,700,000 hemoglobin 124 per cent (Sahli) white blood corpuscles 15,000 platelets 200,000 polymorphonuclears 75 per cent lymphocytes 25 per cent. Blood nonprotein nitrogen was 41 milligrams per liter urea, 36 milligrams creatinine 1 8, and sugar 91 milligrams per liter Wassermann was negative. Her eye grounds and perimeter test were normal. X-ray

is vacuolated as if it contained lipoid, although this could not be determined as no material was available for fat stains The nuclei in general are quite regular, eccentrically placed, rounded or ovoid and with a single nucleolus, although some of the cells have two nuclei Mitoses are present but vary greatly in relative numbers in different areas Many cells seem connected with one another by slender cytoplasmic processes With Laidlaw's silver reticulin stain, the cells are silver positive This tumor shows no attempt at differentiation into the different layers of the suprarenal cortex

Diagnosis carcinoma of the suprarenal gland (cortical type)

CASE 3 (Chart 445624) G C, 16 year old student admitted to the hospital March 14, 1935, complaining of hair on face and body, a deep voice, and no menstruation The patient's father and mother are alive and well The father was born 30 years ago in Italy The mother was born 33 years ago in the United States, of Italian parentage Patient, the second oldest of the 4 children, has 3 sisters living and well. One brother died in childhood of an unknown cause One sister died 2 years ago from a hip infection There is no history of any family illnesses The patient was born in the United States She had measles and chicken pox in early childhood At the age of 12 years she had mumps, and she had a positive Shick test She began her schooling at 5½ years of age and is now in her third year in high school, which is normal for her age She is considered bright, receives good marks, and is considered talented in music She began to menstruate at the age of 13 and had 2 periods a month apart Her hair then was brown, her form and voice girlish After the second period, her hair became thicker and thick dark hair developed on her face, chest, arms, body and legs This has gradually grown thicker and heavier She has not menstruated since the beginning of this hairy growth Her voice has changed, has become cracked and deep, and resembles a boy's "bass" She developed pimples on her face, chest, and back. She has not grown in stature or height since the change in her hair She has had no headaches and no disturbances of her eyes except myopia

The patient states that she is very good in athletics and is strong as a boy, although she is slight She has no change in her affections and is sensitive concerning her present condition and wishes to be like other girls as soon as possible She shaves her face daily

Examination reveals a small, wiry girl with a very heavy black, bushy mop of hair, a "deep blue" partially grown moustache and beard, even though shaven She had hair on chest, arms, and abdomen Her thighs, legs, pubis, and genitalia were excessively hairy The genitalia were practically hidden in a bush Her labia were hypertrophied She had a long clitoris almost 2 inches in length that stood erect like a penis The urine was negative for albumin, sugar and pathological sediment The

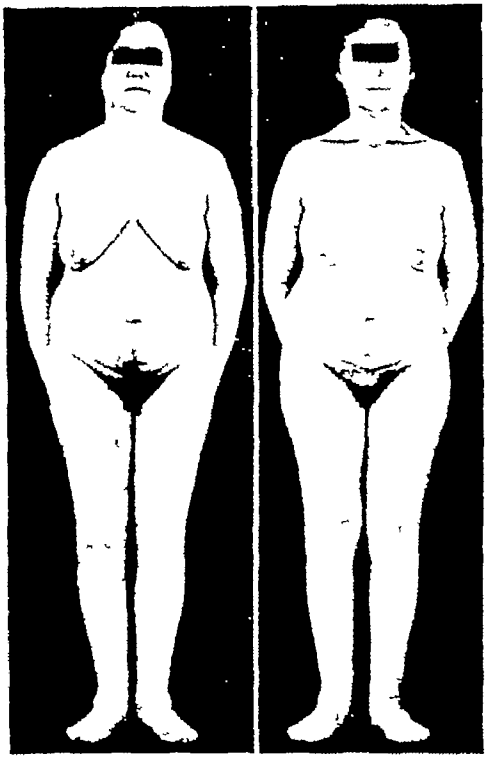

Fig 3 Case 2 Before operation and 2 months after operation, showing change in pubic hair distribution and loss of acne

red blood cell count was 4,900,000, hemoglobin, 90 per cent, white blood count, 11,480 with polymorphonuclears, 73, lymphocytes, 23, eosinophilia 3, transitionals, 1 The blood urea was 16 1, blood sugar 105, blood pressure 138/76

On March 18, 1935, her blood showed carbon dioxide content, 70 1, Cl (as NaCl), 5 9 grams per liter, inorganic products, 3 2, protein, 7 6, sodium, 141 5 milligrams per liter, potassium, 4 7, calcium, 10 2, non-protein nitrogen, 27 The pulse was 68, temperature, 97 4 degrees, weight 47 3, height, 152, body surface, 1 41, basal metabolism —8

On March 20, 1935, pulse was 72, temperature 97 4 degrees, weight 47 3, height, 152, body surface, 1 41, basal metabolism, +1

Eye examination showed a myopia of right 20/100, left 20/70 Her eye grounds were normal as were her perimeter fields

On March 21, 1935, pulse was 68 temperature, 97 degrees, weight, 47, height, 152, body surface, 1 41 basal metabolism, —5

X-ray films taken of her chest were normal, of her abdomen showed the left kidney low, as if pushed down Her right kidney was normal Cystoscopy showed a normal bladder and normally functioning kidneys Pyelograms showed kidneys to all appear-

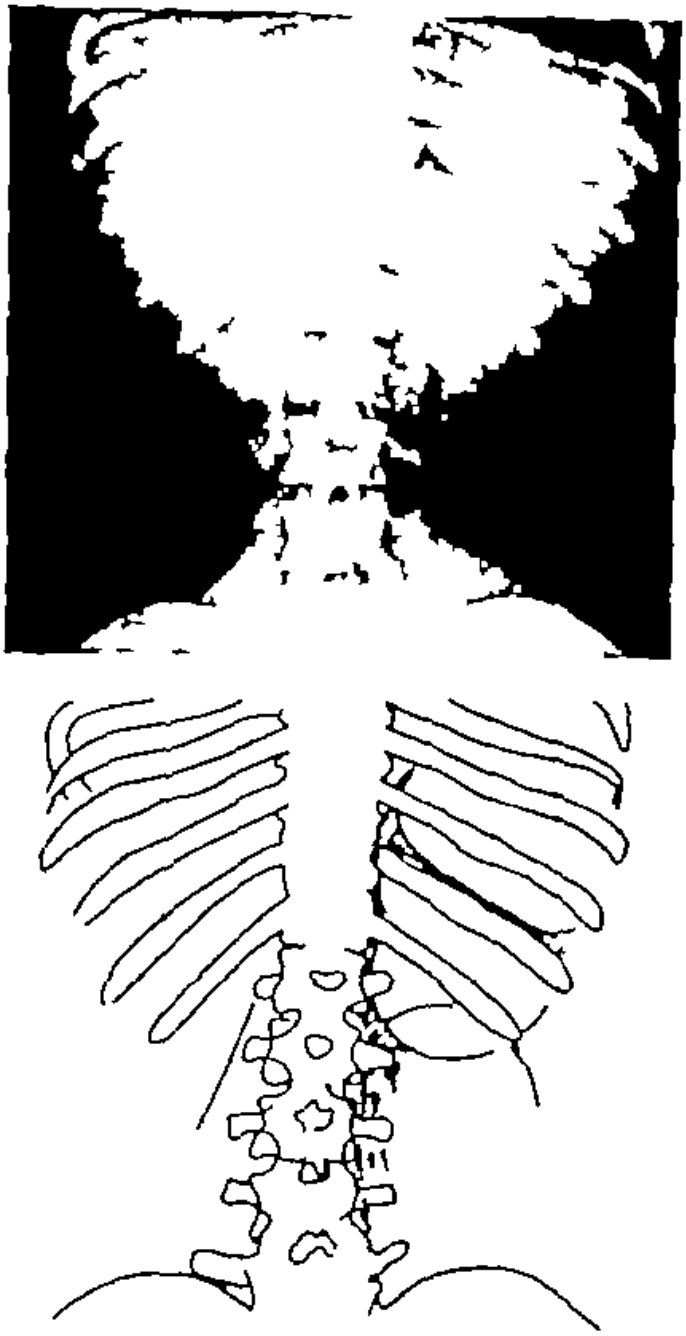

Fig 4 Case 3 Air injection X ray with tracing Shows the air around the left tumor above the displaced kidney

ances normal with the left low but not rotated Roentgenograms taken after the injection of 250 cubic centimeters of air into the region of the left kidney showed a large tumor mass above the left kidney rounded in shape and with a slight notch at the upper pole, and pushing the kidney downward. X ray film taken after injection of 250 cubic centimeters *of air into the region of the right kidney* showed what appeared to be a normal right kidney and an apparently normal adrenal X ray film of the sella turcica appeared normal X ray film of the pelvis and extremities showed that the epiphyses had fused and no cartilage was present. Laryngoscopic examination revealed a male voice with the thyroid cartilage more prominent and with the vocal cords longer than in a girl

April 9, 1935—sex hormone determination of urine showed (1) Follicle-stimulating hormone, negative; (2) Follicular hormone 8 rat units per liter (*This is approximately normal for an adult woman*)

A glucose tolerance test was made March 15, 1935, and showed at 8 a m blood sugar, 95 at 8 30 a m 133 at 9 a m 133 at 10 a m 87 with the urine negative at all times

The patient's bleeding time was 5¼ minutes, and the coagulation time 4 minutes

Chemical analysis of serum on 4-day excess salt diet showed *carbon dioxide content*, 70 1 Cl (as NaCl) 5 9 grams per liter inorganic products, 3 1 protein, 7 6 sodium, 141 5 potassium, 4 7 calcium, 10 2, non protein nitrogen, 27 milligrams

Chemical analysis of serum on 4-day salt poor diet April 2 1935 showed carbon dioxide content 70 8 Cl (as NaCl) 5 9 inorganic products, 3 5 protein, 7 4 sodium, 140 2 potassium, — calcium, 10 2 non protein nitrogen, 27 milligrams

Pelvic examination showed the pelvis to be android with gynecoid characters and moderate sized outlet

April 10, 1935 a left oblique subcostal transperitoneal incision was made and the abdomen was explored The ovaries were very small The uterus was small The right adrenal area was palpated but no certainty was felt concerning its presence There was a large round tumor mass above the left kidney and retroperitoneal Approach to this was made through the posterior parietal peritoneum, and the colon was displaced downward The kidney and the tumor were exposed The tumor was covered with large veins. These were ligated, as well as the adrenal artery and the tumor was then delivered with its fascial planes, and removed There was no injury to the adjacent structures and the tumor was handled very little The posterior peritoneum was closed without drainage as was the incision in the anterior wall Clysis of 2 500 cubic centimeters normal saline solution was given afterward

April 11 the temperature was 103 pulse, 130 blood pressure 158/88 A clysis of 3,000 cubic centimeters normal saline solution was given

April 12 the condition was excellent, she takes fluid well her pulse is 100, and blood pressure 140/70

April 14, temperature was normal condition, splendid blood pressure 120/60

She made an excellent recovery and the wound healed by primary union April 27 injection of air into the right side showed apparently no increase in size of the right adrenal as compared with the former X ray films She was discharged from the hospital May 8, she began to menstruate the first time in 3 years It was quite profuse and lasted 4 days Her voice has become more soprano *Her hair has been coming off her body when bathing* She menstruated the second time at an interval of

29 days after the first period, which also lasted 4 days She is very happy The hair is less and she shaves now every fifth day She menstruated the third time at an interval of 27 days after the preceding period She was photographed for comparison She is attending dances and enjoys her status

Pathological report (56596 Urol No 445624 J C) The specimen consists of paraffin blocks from The Squier Laboratory No 2701 Microscopic examination of sections shows a very cellular tumor which appears to be partially encapsulated and which contains numerous areas of necrosis and some hemorrhage The tumor cells are exceedingly numerous, rather oval or rounded, and somewhat loosely arranged in medullary masses with delicate strands of connective tissue running through them and dividing them into small nests, and occasionally in small, cord-like formations In other areas the cells form rather broad sheets The cells are fairly uniform in size, shape, and staining quality, have round or oval nuclei with a fine chromatin network, and show occasional nucleoli The nuclei are located centrally within the cells The cytoplasm is moderate in amount and rather deeply eosinophilic No mitoses are seen Small capillaries run between some of the nests of tumor cells The larger blood vessels are also seen coursing through the tumor Some of these blood vessels appear to be containing collections of tumor cells In many areas the tumor resembles the adrenal cortex, particularly the reticular zone, and to only a slight extent the glomerular zone Owing to the cellularity, the large areas of necrosis and the presence of tumor cells in blood vessels I believe that this tumor should be considered a carcinoma in spite of the fact that no definite capsular invasions can be made out Sections prepared with the trichrome stain (Fuchsinophil) show the cytoplasm of the tumor cells to be bright red The iron, mucicarmine, Fontana, and phosphotungstic acid stains reveal nothing of note

Diagnosis carcinoma of suprarenal gland (cortical type)

CASE 4 (Chart 450269) I P , a married woman of Russian birth, 36 years of age, was admitted May 12, 1935, complaining of hair falling from her head and an excessive growth on her body Her father and mother are alive and well She has 5 brothers alive and well One brother died in infancy There is no history of family diseases Patient had the usual children's diseases Menses began at the age of 11 years and were regular every 28 days She married at 22 and had two children both difficult deliveries One child is 11 years old, the other 9 years About 6 years ago her menses began to be scanty and then ceased entirely She noticed that about 3 years ago her hair began to grow on her body and face About 2 years ago, the hair on her head became thinner and she began to have hot flashes and frontal headaches She has had no libido for the last 2 years Her appetite is good,

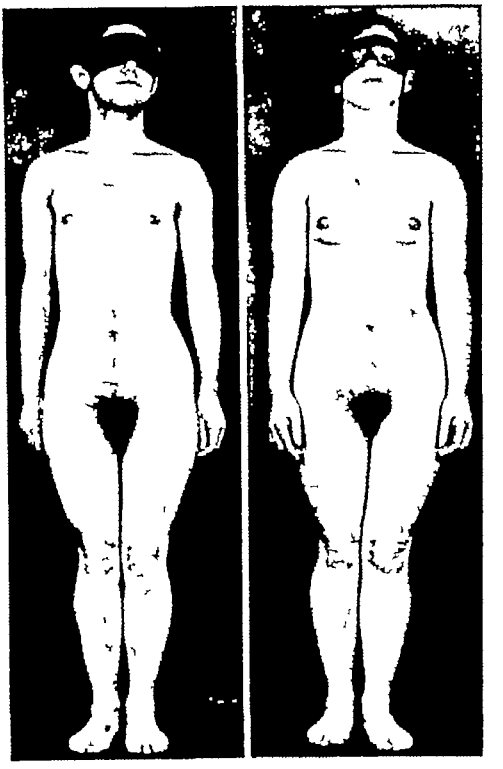

Fig 5 Case 3 Before operation and 2½ months after operation Shows a change in body contour, breasts, and hair distribution

sleep is fair, and she is nervous and fearful She shaves frequently

On examination she was found to be a well nourished woman, rational and voluble The hair on her head was thin but bobbed There was hair on her face but she shaves every few days There was a moderate growth of long hair all over her body but especially around her genitals Her pubic hair distribution was masculine Examination showed marked relaxation of the anterior and posterior vaginal walls and there was a markedly lacerated and hypertrophied cervix The clitoris was very large and resembled a small penis There was some hypertrophy of the labia with deepening of color Her voided urine was normal

May 14, 1935, the patient's temperature was 98, pulse, 84, weight, 63 3 kilograms, height, 152 2 centimeters, body surface 160 basal metabolism —5 Her blood urea was 22 4, sugar 105 and carbon dioxide coefficient, 56 Her red blood count was 4,630 000 hemoglobin, 87 per cent, the white blood corpuscle count was 7,200 with polymorphonuclears 50 per cent, lymphocytes 37 per cent eosinophils 8, miscellaneous 5 Cystoscopy revealed a normal bladder and normal renal function X-ray examination of her chest was negative, of the skull showed a normal

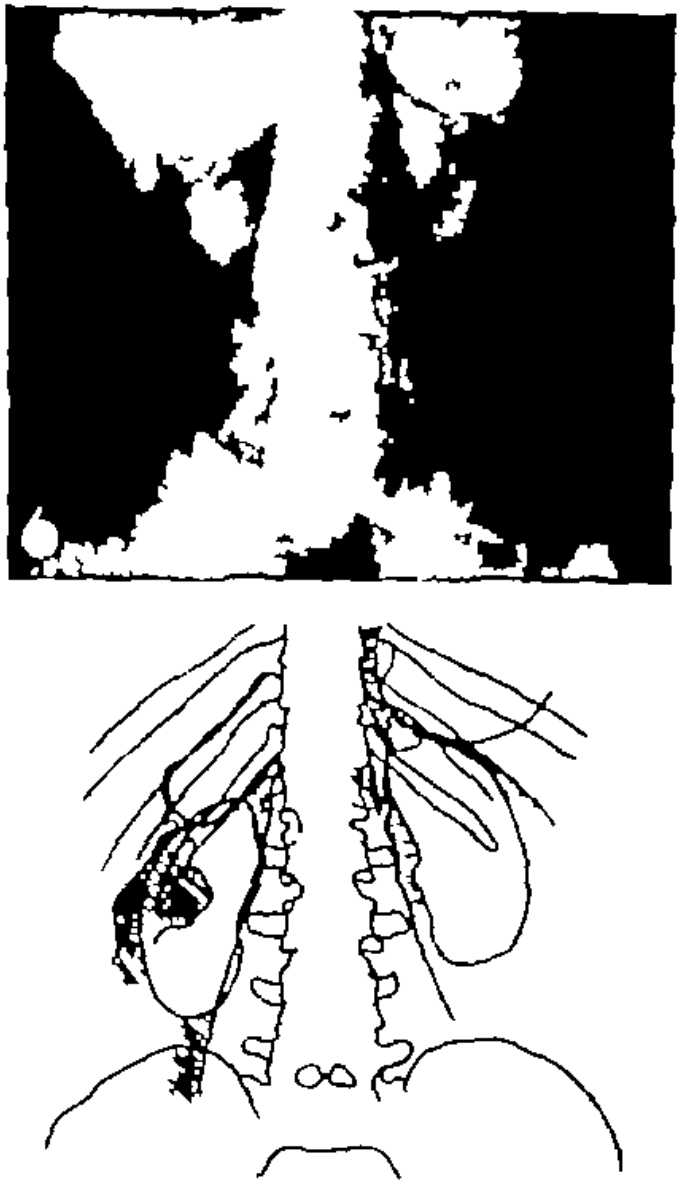

Fig 6 Case 4 Air injection X-ray shows a tumor above the right kidney and a very small adrenal shadow on the left side Died of adrenal cortical failure following removal of right adrenal tumor

sella turcica of the abdomen a low right kidney Pyelographic X-ray showed normal kidneys X-ray films after air injection revealed a rounded tumor of the right adrenal with apparently a small adrenal on the left side

Operation was performed May 27 1935 An oblique right abdominal incision was made and the abdomen was explored The ovaries were very small and hard the uterus felt normal The area of the left adrenal apparently had a mass, shaped and palpable as an adrenal The peritoneum was opened to the right of the duodenum, and the right kidney and adrenal tumor were exposed The vessels were ligated and divided and the right adrenal and its fascia removed including the fascia anterior to the renal vein The peritoneum was closed, and also the wound, without drainage

Her condition was excellent following the operation She was given 3,000 cubic centimeters normal saline subcutaneously After 24 hours, her pulse became rapid and the blood pressure fell to 55/40 She was given a transfusion of 500 cubic centimeters of whole blood and a slow infusion of 2,000 cubic centimeters of 1 per cent saline. Eschatin in a quantity of 2 cubic centimeters was administered every 2 hours Her blood pressure rose to 60/40 but after 4 hours, fell to 50/40 She was given another transfusion of 500 cubic centimeters of whole blood and 4 cubic centimeters of eschatin, with a continuous infusion of normal saline She had difficulty in breathing her blood pressure registered at 50, and with a convulsive attack, she died 31 hours after operation No autopsy was permitted.

Pathological report (No 58597 Urological 450269 I.P) The specimen consists of paraffin blocks from the Squier Urological Laboratory No 2766 Microscopic sections show a very cellular tumor which does not appear to be well encapsulated except along the margin of one portion, where several nests of cells are seen in a thick capsule which resembles cells from the glomerular zone of the adrenal cortex, and do not appear to be part of the tumor The majority of the tumor is composed of large sheets of cells and smaller nests and cords of cells interspersed with delicate strands of connective tissue The tumor cells for the most part are rather large and have pale, vesicular nuclei and indistinct nucleoli These nuclei are usually centrally placed and show no definite mitosis The cytoplasm of the cells is abundant, rather granular pale pink, and in some places appears slightly vacuolated In other places it is slightly foamy The cells vary considerably in size and shape, but to a lesser degree in staining quality Several areas of necrosis and hemorrhage are seen throughout the tumor The tumor is interspersed with larger bands of somewhat hyalinized connective tissue which separates large masses from one another These are infiltrated with tumor cells in many instances There are numerous small and large thin walled blood vessels running through the tumor and, in some areas tumor cells appear to line vascular spaces directly No tumor cells are seen within the blood vessel lumens There is some fat adjacent to the tumor which shows slight infiltration by tumor cells The trichrome stain (Fuchsinophil) shows that the cytoplasm of the tumor cells contain numerous red granules The iron stain shows scattered deposits of hemosiderin in the heavier supportive stroma. The Fontana and phosphotungstic acid stain discloses nothing remarkable The Laidlaw silver stain shows the tumor cells to be silver positive This tumor resembles the adrenal cortex in many places and chiefly the reticular zone of the cortex, rather than the glomerular zone Owing to its cellularity lack of good encapsulation invasion and necrosis, I believe this tumor must be considered malignant

Diagnosis carcinoma of suprarenal gland (cortical type)

Chart Number 16156 The following case was taken from the autopsy records of Presbyterian Hospital

CASE 5 P J R, a male, aged 58 years, was admitted November 3, 1915, complaining of shortness of breath for 1 year Family history was essentially negative except that one sister died following an operation for abdominal tumor Patient had been well until 1 year before admission when he developed an increasing shortness of breath and a cough The cough has increased with the production of a thick sputum occasionally streaked with blood There had been a progressive loss of strength and weight There had been no change in his hair

On examination he showed evidence of consolidation of his right chest with flatness in the lower part The liver edge extended 7 centimeters below the costal flare He had a leucocytosis The prostate was enlarged X-ray examination showed the chest to be filled with metastatic tumor X-ray of the skull showed metastasis in the right parietal region Aspiration of the chest showed on microscopic examination, tumor cells, epithelial cells in character but not diagnostic

On autopsy, he showed a cortical tumor of his right adrenal with metastases to pericardium, endocardium, lungs, liver, kidneys, and retroperitoneal tissues

The following case presented the evidence of pubertas præcox with hirsutism, but without demonstrable evidence of adrenal change by X-ray There was no operative interference

CASE 6 L S (Chart No 379627), a boy aged 11 years was admitted to the hospital May 29, 1933, complaining of dwarfism, excessive hairiness and sexual maturity Father and mother were alive and well There was no history of family abnormalities Patient was the first born to his mother and considered normal up to 22 months of age At that time he began to show evidence of structural changes He began to become hairy at the age of 5 years, and at 7 or 8 years developed adult genitalia He was backward at school, was apt to be moody and although at times was good-natured, he was likely to be sensitive about his condition He was proud of his strength and adult characteristics, and was fond of cigars No sexual history could be obtained from him as he refused to answer all questions

On examination he resembled a muscular achondroplastic dwarf with profuse growth of hair on the face, chest, shoulders, arms, back and abdomen and legs His genitalia were adult Red blood corpuscle count was 4,880,000, hemoglobin, 92 per cent, white blood corpuscle count was 11,500 with polymorpho nuclears 80 per cent, lymphocytes

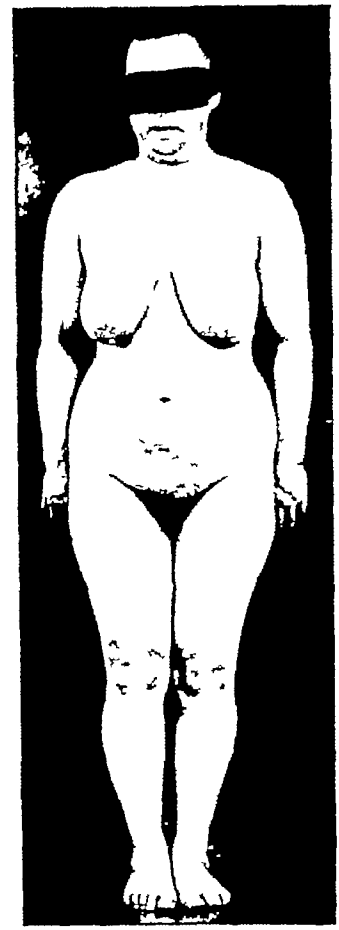

Fig 7 Case 4 Before operation, showing the hair distribution

16 per cent, miscellaneous 4, and basal metabolism plus 10 There was no hypertension X-ray examinations of his skull showed no change from normal Repeated Wassermann tests were negative

Urine hormone findings by Kurzrok

Date	Prolan	Theelin
May 30, 1933	Negative	Negative
May 31 1933	Negative	4 rat units per liter
June 1 1933	Negative	4 rat units per liter
June 2 1933	Negative	4 rat units per liter
June 3 1933	Negative	4 rat units per liter
June 4 1933	Negative	4 rat units per liter
June 5, 1933	Negative	2 rat units per liter
June 6, 1933	Negative	No rat units per liter
June 8, 1933	Negative	4 rat units per liter

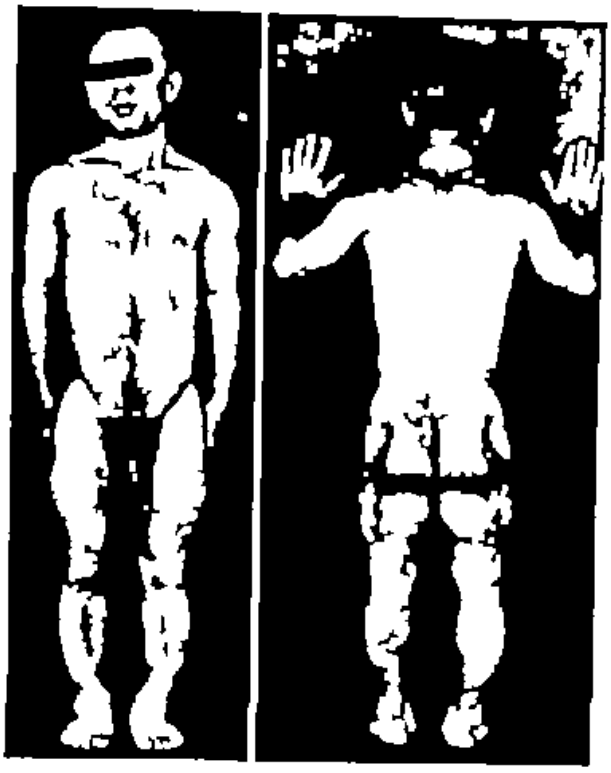

Fig 8 Case 6 A boy of 11 years of age Shows extreme hirsutism and precocious masculinity

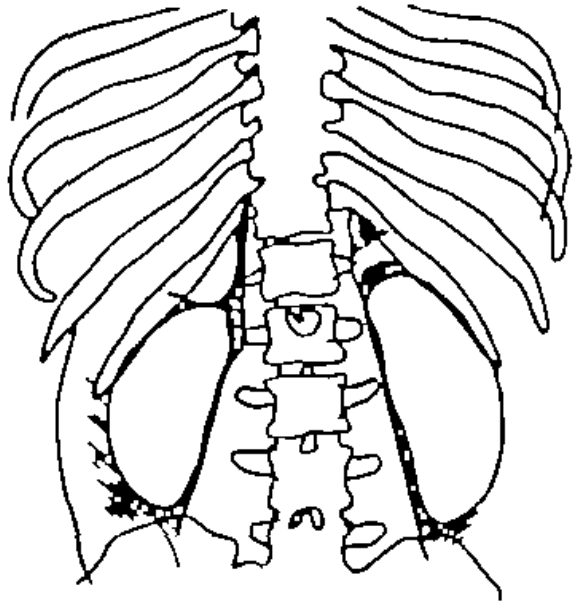

Fig 9 Case 6 Air injection X-ray with tracing No defiant evidence of adrenal tumor A suspicious change on right side This case is not proven to be tumor

Analysis of his blood serum, fasting, was Protein, 7 1 carbon dioxide, 68 2 sugar 90 grams per liter chlorides (as NaCl) 5 79 non-protein nitrogens 25 0 milligrams per liter phosphorus, 3 4 sodium, 136 2 mill-equivalents per liter, potassium 4 8

X ray examination of the chest showed no evidence of thymus Air injections of the adrenals showed the left adrenal to be larger than the right but of normal shape, and not sufficiently changed so that a diagnosis of tumor could be made

The patient was taken home by his mother and no further study was possible in this case

The following case was one in which the diagnosis rested between a basophilic adenoma of the pituitary and bilateral hyperplasia of the adrenals

CASE 7 (Chart 320378) P.S girl 20 years old was admitted to the hospital, complaining of obesity and irregular menses F ther born in Italy was a normal but illiterate laborer Mother was born in Italy There were 6 children The eldest, a female 22 years of age, finished 7th grade in school, the second was the patient the third, a boy 17 reached 7th grade in school the fourth a boy 14 was mentally deficient the fifth child was 12 years of age and normal and the sixth child died in infancy

Patient was of normal birth and had had a normal childhood until 12½ years of age when menses began She began to increase in weight Her menses were regular for 5 months and then ceased They did not recur until 2 years later She developed a tired and sleepy feeling She has had headaches over the eyes and in the occipital region for the last few years There occurred a heavy growth of hair on head eyebrows, and some on her face and chin and on her arms and legs She suffered from chilly feelings and had fainting spells

She weighed 3 1 pounds and was 65 inches in height. She had a heavy growth of hair on her head, some on the cheeks, upper lip and chin There was marked hair on her arms and legs The pubic hair distribution was masculine Her breasts were medium sized and her abdomen was pendulous Wassermann tests were negative Blood urea was

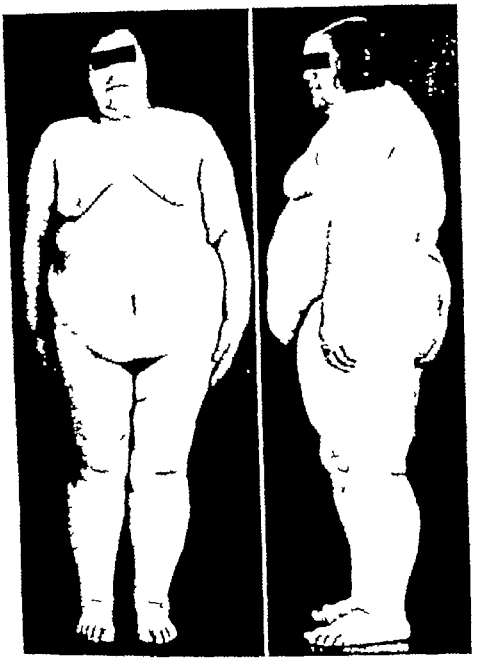

Fig 10 Case 7 Shows obesity and hirsutism

12 milligrams per liter and blood sugar was 97 Basal metabolism rate was plus 22 X-ray film of the skull showed no change in the sella turcica Examination of her eye grounds was negative Psychological determination classed her a "borderline defective" Her blood pressure was 170/30, pulse averaged 90

On February 4, 1933, examination revealed 3 rat units per liter of ovarian follicular hormone in the urine On June 8, 1933, examination revealed 9 rat units per liter of ovarian follicular hormone in the urine Air injected on May 5, 1933, showed both adrenals were remarkably enlarged but apparently of the symmetry of a normal adrenal Patient menstruated for 6 days while in the hospital, receiving 10 cubic centimeters of antuitrin during the week She showed spreading of her teeth suggestive of acromegaly There was no change from normal in the clitoris, labia, or pelvis

No diagnosis was made but it rested between (1) basophilic adenoma of the pituitary, and (2) bilateral hyperplasia of the adrenals

CASE 8 (Chart 451144) B W, a girl, 23 years old, was admitted May 7, 1935, complaining of hair on her chest Family history was negative except for 1 sister who has excessive hair on her body similar to the patient This girl is 15 years old Patient had had an apparently normal childhood except for empyema Her menses began at 12 years and are of the 28 (5 to 7) day type The flow is normal, with no disturbances up to the last period which she

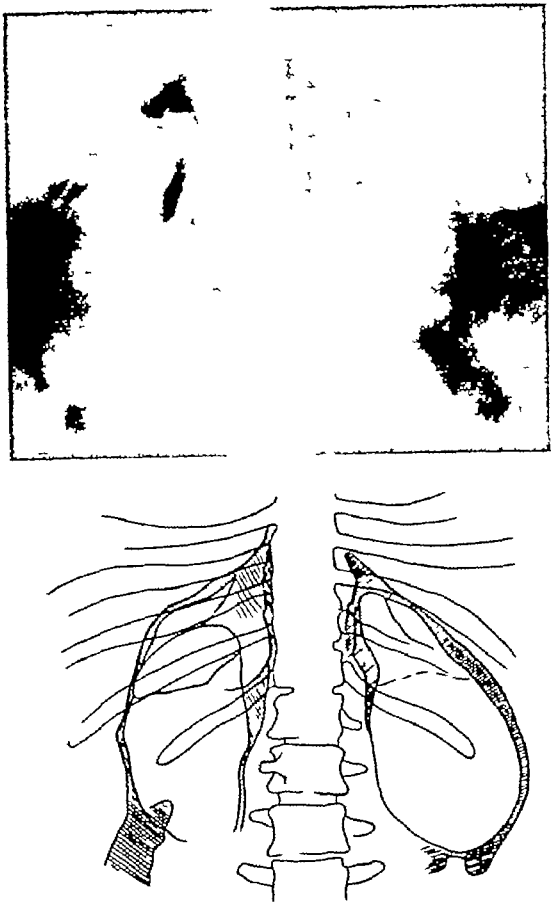

Fig 11 Case 7 Air injection X ray with tracing There is apparently a hyperplasia of both adrenals

missed without any known cause Since she was 13 years old, she has had a gradually increasing black hairiness of the chest arms and legs, and also of her face

Examination showed a well nourished body She was bright She had long black hair on lips, chin, chest, abdomen, legs, and arms The pubic hair was thick and masculine in character There was no change from normal in the clitoris, labia, or vestibule She had no hypertension Her blood examinations were normal Cystoscopy was essentially negative X-ray of the skull was normal X-ray of the chest showed evidence of an old empyema with operation on the right side Air injected into her perirenal spaces did not reveal any change in the adrenals suggestive of hypertrophy or tumor A pelvic examination did not reveal any demonstrable change in her uterus or ovaries from the normal

CASE 9 (Chart 452126) L Z, a Jewish girl 21 years old, was admitted May 27, 1935, complaining

of nervousness and abnormal hair distribution, for 1 year Family history was negative Patient had had a fairly normal childhood. Her menses began at 14 years but have never been regular They are now very scanty and she misses several months at a time She has lost weight in the last few months She has been very unstable emotionally She has had to shave the hair that appeared on her face and arms On the thighs and legs the hair is long and black. The hair on her abdomen pubis and genitalia is thick and masculine in distribution She has no hair on her chest.

Examination reveals normal pelvic organs, with no change in the clitoris or labia. There was slight hypertension 140/80 Her blood count showed red blood corpuscles, 5,300,000 hemoglobin, 95 per cent white blood corpuscles, 11,800, with polymorphonuclears 87 per cent. Her basal metabolism was minus 7 Wassermann tests were negative X-ray films of her skull and chest were negative. Her blood chemistry examinations were essentially normal Her urine on examination by Dr Kurzrok showed (1) 8 rat units follicular hormone per liter (2) follicle stimulating hormone not present. Air injected around both adrenals did not show any change in the adrenals that would warrant a diagnosis of hyperplasia or tumor

The following case presented the symptoms of hirsutism and more or less disturbance of menstruation but no demonstration of adrenal tumor and no operative interference.

CASE 10. (Chart 448506) B.A G a married woman 30 years old, was admitted on March 3 1935 complaining of pain in the right flank with dysuria and frequency She also had dyspnea on exertion, increase in weight and in growth of hair on her body face, arms, and legs Her family history was negative. Patient had had a normal childhood She began to menstruate at 12 years of age Periods increased in amount up to her marriage at 20 years of age. She has 1 child 4 years old. For the last year her menses have increased, lasting 11 days or so and for a period of 3 to 4 months, it appeared daily During this time the hair appeared on her face, arms, abdomen, and legs. She shaved her face and abdomen to make them appear feminine

Examination revealed a stout young woman with pendulous breasts She had hair on lip and chin a male distribution of pubic hair and increased hair on arms and legs. There was no hypertension Pelvic examination showed hypertrophy of labia and clitoris with no palpable masses in the fornices or change in the uterus Her blood count and blood chemistry were normal Her urine showed pus, and cystoscopy with pyelographic studies revealed a colon bacillus cystitis X-ray films of her chest and skull were negative Air injected around both adrenals did not show any change that would warrant a diagnosis of increase in size or of tumor of the adrenal

OBSERVATIONS

Hypertension occurs in many cases This has been reported in the continuous type and is usually associated with a more rapid heart beat than normal In our Case 2 the pulse rate was consistently over 120 beats per minute. The blood pressure was between 160/110 and 195/105 The high systolic readings in the 4 patients operated upon in order were 155 195 138 and 150. From cases in the literature the systolic reading varies in a wide range, rising rapidly with exercise and falling rapidly with rest. The hypertension of tumors of the adrenal medulla manifests itself more frequently in the paroxysmal type, associated with palpitation, weakness, dyspnea and fainting during the attack, and with symptoms of pulmonary edema, and frequent death. A most interesting case of paroxysmal hypertension has been reported by Porter and Porter in which an adrenal tumor successfully removed was pathologically reported by Ewing as cortical tumor of the adrenal Why this should have produced these symptoms is not clear

Of interest has been the association of the redness and duskiness of the face and hands with polycythemia. A case reported by Hunter McMillan Boyd and Cameron, had a red blood count of 5 570,000 and a hemoglobin of 109 per cent A case of Khavine had a red blood count of 5 500,000 The case of Kayser and Walters had a red blood count of 5,290 000 and a hemoglobin of 80 per cent. Zucker reported a case with a red blood count of 10 500,000 Only one of our patients (Case 2) showed the redness and duskiness, and it was the only case with polycythemia. Her red blood count was 5 700,000, and her hemoglobin was 124 per cent by the Sahli method. The blood counts of the other cases with definite tumors, showed no change from normal.

The blood count in the cases of virilism but without proved tumors showed no change from normal except in the case in which the diagnosis rested between adrenal hyperplasia and basophilic adenoma of the pituitary (Case 7) and in this case the red blood count was 5,300,000 and the hemoglobin was 95 per cent

Basal metabolism tests showed results which probably had a bearing only on the general endocrine state and not specifically on the adrenal situation The reports showed

Case 1, not done
Case 2, +31 (case of obesity and low sugar tolerance)
Case 3, +1
Case 4, — 5
Case 7, — 7 (case of pituitary-adrenal uncertain diagnosis)

The chemical analyses of the various bloods showed no change from normal, or with some change from known causes not apparently related to the adrenal dysfunction Only 1 patient showed low sugar tolerance (Case 2) Studies of the blood in these cases by Loeb, showed no abnormalities from normal in chlorides, inorganic phosphorus, sodium, potassium, or calcium

Studies in the sodium chloride balance revealed no change from normal There was no evidence that these cases had the opposite of the low balance seen in Addison's disease

In 1 patient (Case 3) an air injection X-ray picture of the remaining adrenal, 30 days after successful removal of the tumor, showed an apparently definite increase in size of the shadow of the remaining adrenal (Fig 20)

The report of Dr J J Pfiffner who so kindly analyzed the tumor in Case 3, was quite interesting He stated

A fraction from the tissues was prepared and assayed on the adrenalectomized dog for the cortical hormone (life maintenance factor) I was unable to demonstrate the presence of the life maintenance hormone The quantity of tissue available in work of this character is always a limiting factor We can conclude from our data, however, that the concentration of the cortical hormone in this adenoma was less than 20 per cent of the concentration of the hormone in the normal beef adrenal cortex No comparison can be made with the normal adrenal since no data on this point are available It seems to me that these observations speak against the possibility of an excessive secretion of the cortical hormone (life maintenance factor) occurring in this case of virilism In the course of separating the cortical hormone fraction from the adenoma, fractions were obtained which should have contained the sex hormones if they were present These fractions were turned over to Dr Kurzrok

Three suggestions have been put forward by Collett for these sexual changes (a) The adrenals act directly on the gonads (b) The adrenal cells retain their primitive sex function and produce changes themselves (c) The adrenal cells stimulate the anterior lobe of the pituitary which in turn acts on the gonads He was of the opinion that suggestion (b) based upon investigations by Laulaine and confirmed by A Kohn and Brachet, held the strongest consideration, and that the medullary and testicular part of the ovary are closely connected at an early stage with the suprarenal gland cortex and should be involved with the suprarenal cortex during further development When this change occurs in the suprarenal cortex, it is accompanied by secre-

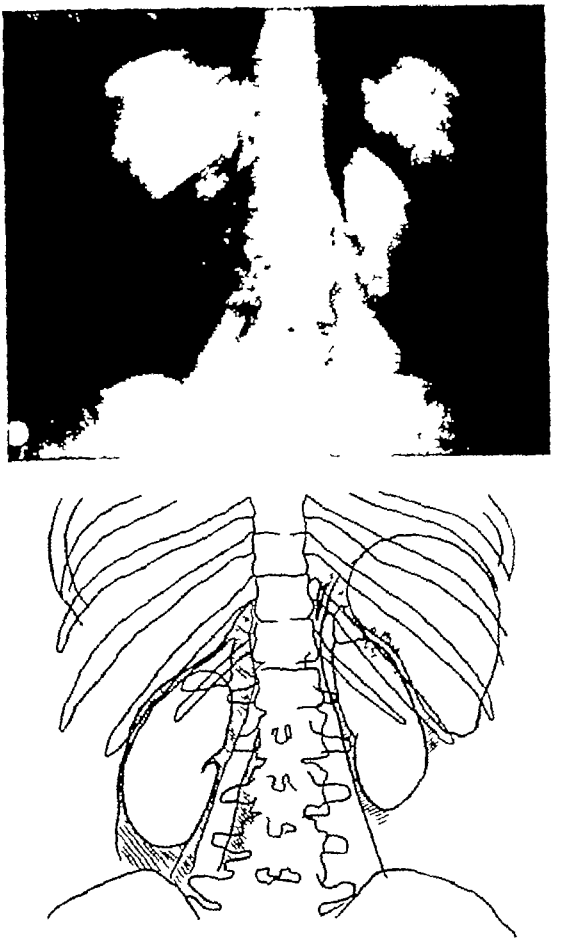

Fig 12 Case 8 Air injection X-ray with tracing There is apparently no evidence of adrenal tumor in this case of hirsutism.

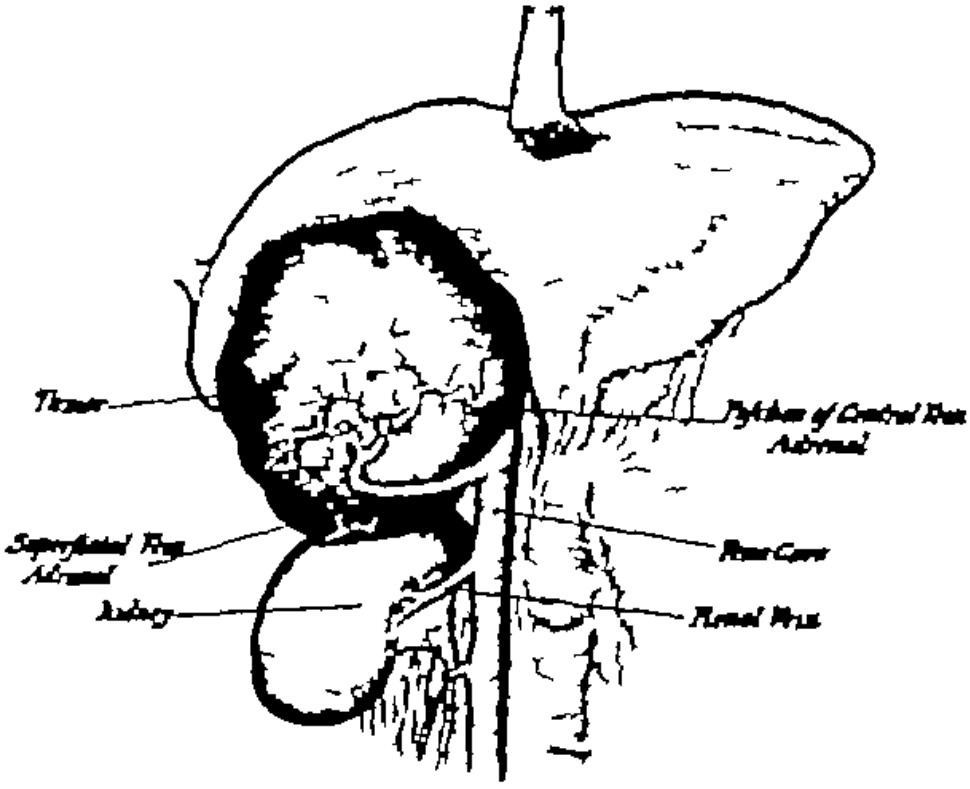

Fig 3 Case 2 A drawing of right adrenal tumor showing venous channels

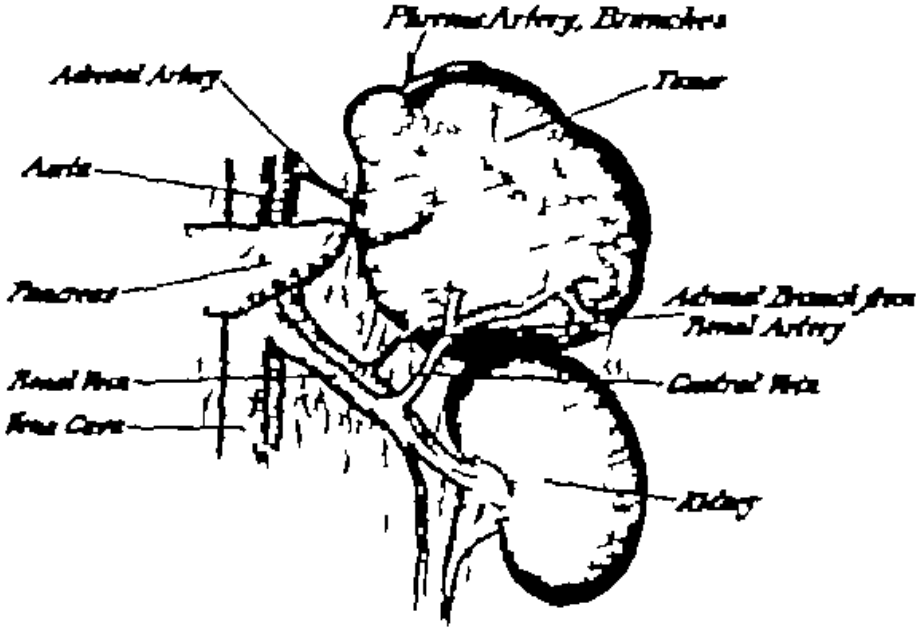

Fig 4 Case 3 A drawing of left adrenal tumor showing the blood supply

tion from these testicular cells and through the testicular hormone masculinization I produced Examination of the ovaries in reported cases, however apparently showed no change except atrophy

The histology of these tumors showed a variation between the case without endocrine symptom and those with endocrine symptom In Case 1 with no virilism the tumor had a varied morphology with an area of cords of epithelial cell reminiscent of all the layers of the adrenal cortex The zona

Fig 15 Case 1 Photomicrograph of a portion of the tumor where the cells tend to form structures reminiscent of the zona fasciculata of the suprarenal cortex

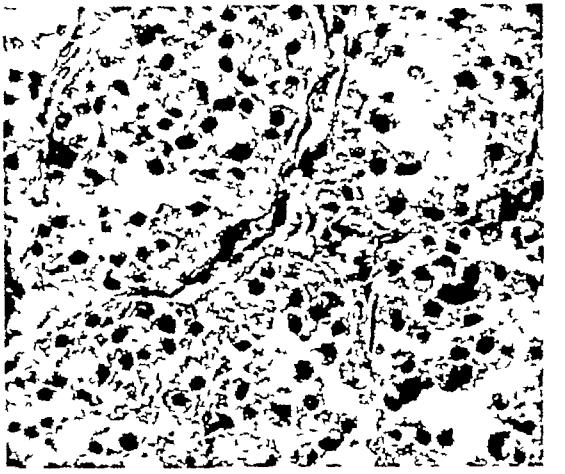

Fig 16 Case 2 Photomicrograph of a representative area of tumor tissue showing masses of tumor cells with granular faintly acidophilic cytoplasm separated by delicate septa with capillaries

fasciculata type of arrangement perhaps appeared in preponderance with fewer areas resembling the reticularis, and only occasionally, an area resembling the glomerulosa In the remaining cases all with virilism the resemblance to the reticular zona was more apparent with only a few areas resembling to a slight extent the glomerular zone

This apparent variation of the cells of the tumors is of special interest in view of the work of Brostner and Vines in which they found vivid red granules stained by fuchsin in the cytoplasm of adrenal cells in cases of virilism Since the fuchsin granules were

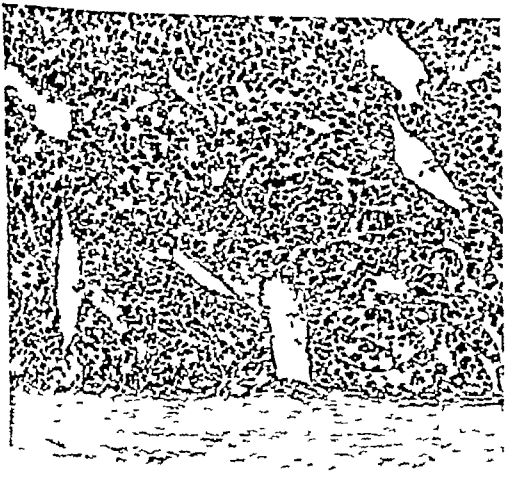

Fig 17 Case 3 Photomicrograph of tumor near the capsule. Shows areas somewhat resembling the reticular layer of the adrenal.

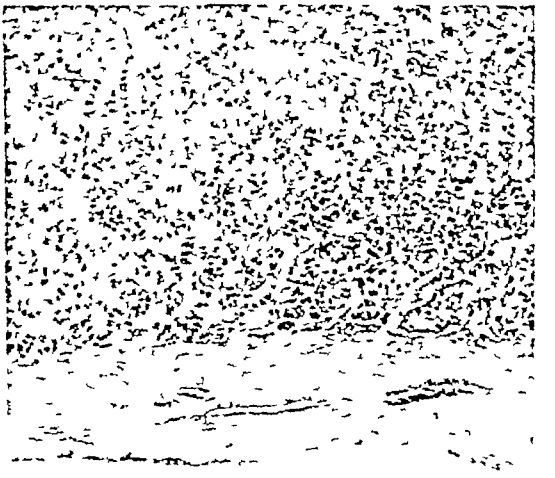

Fig 18 Case 4 Photomicrograph of tumor near the capsule Areas resembling the reticular layer are shown

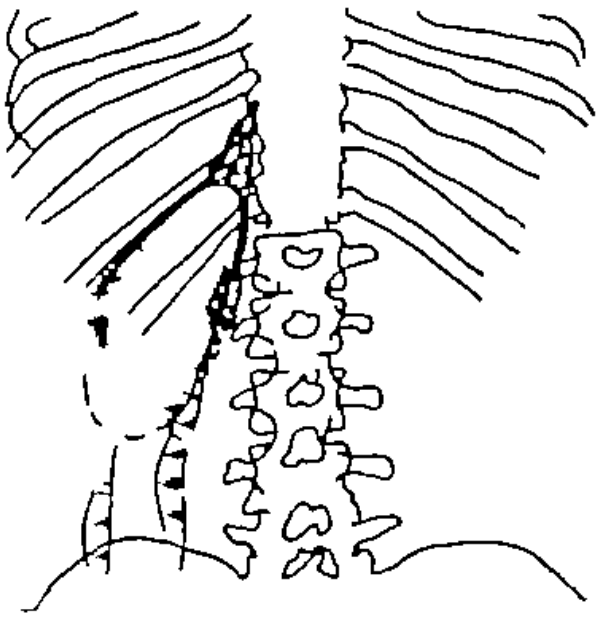

Fig 9 Case 3 Air injection X ray with tracing of the normal right adrenal before operation

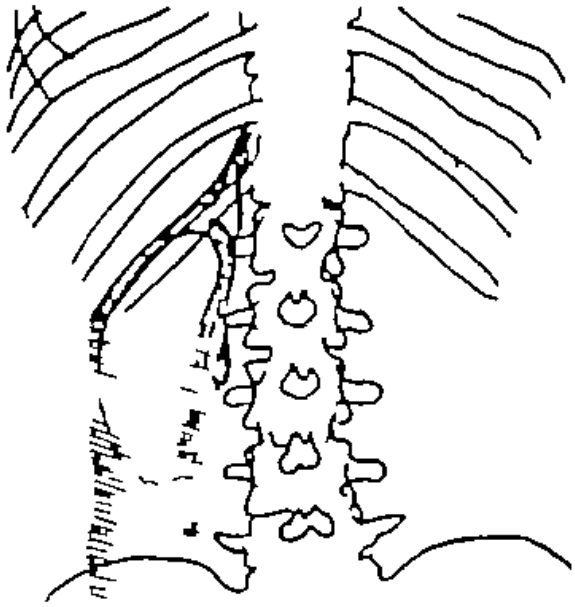

Fig 10 Case 3 Air injection with tracing of the normal adrenal month after operation The adrenal shadow has apparently increased in size over the shadow in Figure 9

found in the reticular layer of the adrenal the assumption arose that the increase in cells and the increase in size of these adrenals was due to a change in the reticular layer Goldzieher and Koster called attention to the importance of this observation and confirmed these findings. They stated that the microscopic examination of the adrenals in 5 cases of hirsutism and obesity without tumor showed the formation of an unusually broad reticular layer of the cortex. This layer stood out not only for its abnormal width but also by the intense staining of the cell bodies with eosin

Broetner and Vines collected from various sources material from 8 cases of cortical carcinoma and reported verification of the association of clinical virilism with fuchsinophil granules in the adrenal cells. They associate the presence of the fuchsinophil material with the masculinization of the female although there is no proof that the material is the actual hormone which causes sex reversal. The fuchsinophil substance was

reported absent in growths which were not accompanied by sexual changes

With the Masson trichrome stain which is identical in all details to the fuchsinophil stain described by Brostner and Vines, these tumors showed relative degree of this reaction (Table I)

TABLE I

Case	Surgical Path. No	Fuschsinophil reaction	Virilism
1	36423	1+	None
2	47864	4+	1+
3	58506	4+	1+
4	58597	3+	1+

For comparative controls to determine the amount of fuchsinophil granules and with estimations in relation to the amount of the tumor cells, we found (1) Normal adult dog adrenal, ½ hour post mortem, 2+ reaction, (2) normal human adrenal, 3½ hour post mortem, 2+ reaction, (3)[1] normal human adrenal, 13½ hours post mortem, 3+ reaction, (4) normal human adrenal, 12 hours post-mortem, 2+ reaction, (5) normal human adrenal, 7 hours postmortem, 4+ reaction

The dog adrenal showed most of the fuchsinophil reaction to be in the cells of the reticular zone of the cortex, less in the fascicular zone, and practically none in the glomerular zone There were cells scattered throughout the reticular zone that took the reaction very strongly, but the majority of the cells took it only faintly The nuclei were slightly darker than the majority of the cells in this zone with the trichrome stain, but when stained with hemotoxylineosin, no difference was made out The human control adrenals showed this only to a very slight extent

This study apparently did not show the striking contrast between the tumors and the normals as controls, as did the reports of Brostner and Vines Definite increase in these granules was present, however, scattered throughout the tumor areas The importance of these findings of the function of the reticular layer of the adrenal cortex and of the presence of the increase of the fuchsinophil granules with hirsutism is somewhat increased by the experiments of Miller, Deansley and Whitehead, who demonstrated an enlarged reticular layer of the adrenal cortex in the immature female rodent, and connected this "Zone X" with the influence of the adrenal cortex on the functions of the sex glands Goldzieher considers the enlarged reticularis in the patients with obesity operated upon to be due to an exaggerated Zone X as regards both configuration and staining properties

In all the tumor sections, the presence of lipoids was apparent The Laidlaw silver stain showed that the tumor cells in all the cases were silver positive and did not form reticulin The Fontana and phosphotungstic acid stains revealed nothing of note In one patient (Case 4), the iron stain showed deposits of hemosiderin There were no nerve fibers

[1] This adrenal contained an adenoma in addition to the normal tissue It was an incidental finding at autopsy in a case without any symptoms or signs of virilism

CONCLUSIONS

1 Adrenal cortical tumors may occur without virilism

2 Adrenal cortical tumors may occur with endocrine changes as follows (a) pseudohermaphroditism (female), (b) premature puberty in the male, (c) growth maturity with masculinity in female children, (d) hirsutism, amenorrhea, and adiposity in adult females, (e) after menopause, an indistinct picture with adiposity, (f) possible inversion changes in male adults

3 The adrenals may be adequately shown by the X-ray after air injections

4 A possible diagnostic urine hormone is present

5 Removal of adrenal tumors by the transperitoneal route is surgically better

6 A percentage of cases of collapse following the removal of the adrenal

7 As yet control of the collapse by cortical hormone is experimental

8 Removal of the tumor produces a symptomatic cure of the endocrine symptoms but has no effect on the anatomical changes in the pseudohermaphrodite

9 The metastases of these tumors produce the same endocrine changes as the original tumor

10 The tumors that produce the endocrine changes have cells which resemble most the reticulate layer of the adrenal and have an increase in fuchsinophil granules over the normal

11 Adrenal cortical hormone known as cortin has not been demonstrated in these tumors

12 A sex or virilism hormone of these tumors has not yet been proved to be present

I wish to express my great indebtedness to Dr J Bentley Squier director of the clinic, for his guidance and helpfulness in this study Thanks are given to Dr J J Pfiffner for his careful work on the life maintenance factor to Dr W C von Glahn for his loan of materials and to the rest of the staff of the urological service for their material, their suggestions, and their cooperation

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Discussion

Dr H Lisser, M D, San Francisco Dr Cahill's presentation is timely Recent years of illuminating research in experimental biochemical laboratories the world over have unfolded multitudinous discoveries of incretory functions and interglandular relationships, much of which engages the rapt attention of the endocrinologically minded clinician A quickened interest has been roused in hormonal tumors, whose excessive or perhaps perverted production of this or that secretion, creates remarkable endocrine syndromes As Cushing aptly phrased it many years ago in discussing hypophyseal disturbances, if it had not been for the factor of tumor "*blowing itself into clinical prominence*, our knowledge of the pituitary body might have been delayed far longer And the surgeon including the neurosurgeon, the urologist and the gynecologist, has become aware of the great service he may render by

skillful removal of endocrine functioning tumors One need but mention the spectacular relief from attacks of paroxysmal hypertension, by removal of an adrenal medullary paraganglioma, or the cessation of hypoglycemic fits of coma by enucleating a Langerhans island adenoma, or the restoration of calcium to the moth-eaten skeleton of an osteitis fibrosa cystica by similar excision of a hyperfunctioning parathyroid adenoma, or the transformation of a masculinized female into a refeminized woman by removal of an ovarian arrhenoblastoma

The adrenal cortical tumors are equally fascinating in their production of bizarre endocrine manifestations pseudohermaphroditisms, sexual precocity, sexual inversion, masculinization of the adult female as in virilisms and hirsutism, and feminization of the adult male with gynecomastia, etc We are grateful therefore to Dr Cahill and all others who record their clinical observations, for we need larger experience to aid us in earlier diagnosis and to improve our judgment of the wisest therapy We must become more surgically minded toward these genitosuprarenal syndromes, not only in regard to tumors when indications for surgery are obvious, but also in cases in which quite similar symptoms and signs are due to hyperplasia It must be increasingly realized that the size of a ductless gland is not necessarily an index to its function The larger goiters are ordinarily associated with diminished thyroid activity We are long since accustomed to practice subtotal thyroidectomy for hyperplastic hyperthyroidism even though the gland itself be enlarged only slightly And until a now unpredictable method is evolved for combating overproduction of an internal secretion, we must resort to the cutting away of most of the overfunctioning tissue

The most formidable difficulty encountered in pinning the diagnosis to adrenal cortical overactivity occurs in those cases, the great majority, in which no mass can be felt and in which retrograde pyelography also fails to reveal a tumor I am especially impressed therefore with the aid Dr Cahill has obtained by utilizing the injection of air into the perirenal fascia in order to visualize the adrenals by X-ray This diagnostic maneuver would seem to be of the utmost importance not only in recognizing tumors too small to feel, yet not large enough to distort the pyelogram, but also in detecting hyperplasias, and in the case of large tumors, in obtaining some notion of the size at least of the supposedly normal adrenal

However, if enlarged adrenals were found by this method, there would be some who would contest their responsibility for the syndrome, preferring to assume that the hyperplasia was secondary to the so called "pituitary basophilism," as claimed by Cushing Such difference of opinion could be settled only by subtotal bilateral adrenalectomy, if the syndrome vanished thereby, it would be reasonable to consider the adrenals as the primary cause After all they are simpler to explore than the hypophysis I am interested in the transperitoneal approach, the technical merits of this as compared with the customary renal incision from behind is not one which the internist is qualified to discuss, but it would seem to possess one advantage—it might permit a view of or at least palpation of the pelvic organs and thus exclude an arrhenoblastoma

The differentiation of adrenal cortical virilism (with amenorrhea, heterosexual hypertrichosis, perhaps obesity and hypertension) from Cushing's disease, arrhenoblastoma, and possibly, oat-cell thymus tumor, presents considerable difficulty if a tumor cannot be demonstrated as in the case of the pituitary, thymus and adrenal, by X-ray, as in the case of the ovary, by palpation. Whether hormonal studies of blood and urine will prove helpful remains a question for the future At first thought it appears odd that a condition suppressing female functions should be associated with an excessive outpouring of female sex hormone in the urine. A paper (not by the writer) is to be published shortly, reporting excessive amounts of male hormone in virilism, a finding more in harmony with the clinical picture

Whatever adrenal secretion is responsible for these extraordinary endocrinopathies, it is certainly not the medullary hormone, suprarenalin, nor the "indispensable to life" hormone, cortin These sex abnormalities have not been reproduced experimentally by long continued overdosage with these substances

It is to be hoped that some day we will be able to assay an individual's hormones quantitatively in blood or urine or elsewhere To a limited extent this is possible even now But when this can be done accurately for each hormone of each ductless gland, endocrine diagnosis and endocrine therapy will become vastly more precise and dependable Meanwhile, however, we should familiarize ourselves with well established endocrine syndromes, for brilliant cures can be achieved even now.

SURGERY IN ITS RELATION TO HYPERTENSION[1]

ALFRED W ADSON, M.D., F.A.C.S. WINCHELL McK CRAIG, M.D. F.A.C.S. AND GEORGE E. BROWN, M.D., Rochester, Minnesota

ESSENTIAL hypertension is characterized by an abnormally high blood pressure, which under excitement and physical strain frequently rises suddenly to high peaks. It develops most frequently in young people in the third and fourth decades of life but it also may develop in the first, second and fifth decades. Its progress may be slow moderate, or rapid terminating life at 10 to 15 years after onset if its progress is slow at 3 or 4 years, if moderate and at 18 months, if rapid. Etiologically essential hypertension is probably due to a fault in the neurogenic endocrine vascular mechanism, since no other apparent etiological factors can be demonstrated. The vascular mechanism of individuals developing this disease appears to respond excessively to normal stimuli, an observation confirmed on examination of the blood pressures of children of parents with essential hypertension.

The appearance of low blood pressure in Addison's disease and the report of cures following the removal of isolated suprarenal tumor (20) with the sudden drop in blood pressure following administration of spinal anesthetic has aroused the imagination of the surgeons and encouraged them to attempt surgical procedures to decrease endocrine secretion or to paralyze the vasomotor control over large vascular areas by various forms of rhizotomy or sympathectomy (1 2 3 5 7 8) We have employed a number of surgical procedures and herewith submit a report of these procedures and the results obtained The interval following these operations is still too short to justify drawing definite conclusions, but the results which have been obtained to date suggest that surgical measures will probably come to play an important rôle in the treatment of essential hypertension. The inadequacy of medical treatment has further justified surgical investigation and attempts at surgical treatment

ETIOLOGY

Physiologists have shown that endocrine secretions, particularly those of the suprarenal, pituitary and thyroid glands, play important rôles in maintaining vascular tone Though these secretions are important, it appears that the autonomic nervous system, particularly the sympathetic, plays an equally important rôle in the maintenance of vascular tone. The autonomic nervous system in normal individuals acts as a regulator or governor of the neurogenic-endocrine vascular mechanism. It stands in readiness to call out such reserves as the endocrine secretions, stored energy-giving substances, and it raises the blood pressure to facilitate the increased metabolism to meet the additional mental and physical demands. It alters the homeostasis and prepares the body for flight or fight (Cannon)

Excessive mental and physical demands may cause this regulating mechanism to break down and, unless the condition is recognized early and steps are taken to reduce the strenuous activity of the individual, the disease will continue to progress In other instances the disease does not seem to originate from excessive physical or mental demands but appears to be the result of a faulty autonomic nervous system At the onset the elevated systolic and diastolic blood pressures are of no particular significance, but as the continued load is carried by the cardiovascular mechanism damage results, first in the peripheral arteries and then in the arteries and musculature of the heart. Symptoms, such as headache and precordial distress, together with those of chronic nephritis, retinal hemorrhages, papilledema, and cerebral hemorrhages, appear in order until death results

Hypertension in later life past 50 years of age, may slowly increase, with a corresponding development of arteriosclerosis. It should be borne in mind, however that arteriosclerosis may just as often develop, and result in cardiovascular and cerebral degeneration without the presence of hypertension

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There are numerous other factors capable of producing increased blood pressures, but they should not be confused with the syndrome of essential hypertension, since in these instances definite pathological factors are responsible for the hypertension For instance, the hypertension resulting from hyperthyroidism, suprarenal tumors, basophilism, and eclampsia may readily disappear and the pressures return to normal when the thyroid gland has been resected, the suprarenal tumor removed, the basophilism relieved by resection or by roentgen therapy of the pituitary gland, or when suprarenal hyperplastic tissue has been removed or the gravid uterus evacuated Arteriovenous aneurism, stenosis of the aorta, and glomerular nephritis can also produce hypertension, but unfortunately the pathological factors cannot be relieved as easily as those produced by hyperthyroidism and suprarenal tumor

SYMPTOMS AND CLASSIFICATIONS

Increased blood pressures may become well advanced before the patient is aware of an existing hypertension Insurance examinations often are the first to disclose that such abnormal pressures exist The development of symptoms follows a rather definite course Hypertensive individuals are energetic, strenuous, and ambitious creatures who may not complain of any discomfort until headaches result from excessive mental exertion and fatigue Accompanying this early symptom, the disposition of the individual may change, and he or she may become irritable and complain of insomnia Precordial distress or a consciousness of cardiac action, with a sensation of tumultuous cardio-arterial action, soon follows the appearance of the headache The continuation of these prodromal symptoms varies Sometimes they appear fairly late in the disease and may remain more or less continuous, while again they occur intermittently and make their appearance during sudden, and but temporarily sustained, high blood pressures as long as the individual is subjected to the particular mental or physical strain which has initiated the paroxysmal attack

Dr Wagener, on observing the fundi of patients suffering from hypertension in its various stages of progress and with its varying degrees of blood pressure, has observed that the retinal arteries present correspondingly varying states of spasm, namely, less spasm and larger retinal arteries in the earlier stages, with slow progression of symptoms, and, in the later stages and in patients with a rapid progress of the disease, the reverse We would naturally expect a destructive process, a sclerosing one, to follow the one of spasm This suspicion has been corroborated by Wagener, inasmuch as certain branches of the retinal artery may vary in caliber due to spasm while others remain fixed apparently due to a sclerosing process Retinal hemorrhages, flame-like in shape, occur fairly early in the course of the disease, but papilledema occurs only when the disease is well advanced or the progress is extremely rapid

As the disease progresses, damage results in the cardiovascular mechanism similar to that which has been observed in the retinal arteries Chronic nephritis develops, coronary sclerosis with accompanying myocardial changes, and coronary occlusion, may suddenly terminate the life of the individual In some instances, cerebral symptoms, such as degeneration, with accompanying mental deterioration or vascular occlusion or rupture with the resulting monoplegias, hemiplegias, and epileptiform seizures, may occur The arterial damage likewise affects the function of visceral organs and peripheral arteries of the extremities, but the compensatory factors appear to be more capable of adjusting the situation than are those controlling the circulation of the heart, kidneys and the circulation of the retina and brain

Numerous investigators (4) have attempted to classify patients into groups relative to the progress of the disease, but none has presented a more workable group than Keith (16), with the collaboration of Wagener and of Kernohan Kernohan conducted pathological studies of arterioles in innumerable biopsies taken from the pectoral muscle of patients suffering from essential hypertension He has definitely demonstrated hypertrophy of the media, and in some cases thickening of the intimal lining Keith and Kernohan, and Keith, Barker and Kernohan, then collaborated in a study to learn if there existed a ratio between the

lumen of the arteriole and the thickness of the vascular wall. After analyzing 100 cases they stated that there did exist a definite decrease in the lumen of the arterioles, in addition to a thickening of the walls, in comparison with specimens for biopsy from patients who were not suffering from hypertension. They found that in a normal small artery or arteriole, the ratio of the lumen to the width of the wall is about 2 to 1 This ratio decreases with the advance of the disease, and in the rapidly progressing cases of essential hypertension, the ratio changed from the normal of 2 to 1 to 1 to 1 indicating that the lumen either has been reduced in size by the contracting process of the medial muscular layer or that there actually has been hypertrophy of the media and intimal layers of the arterial walls. One can speculate concerning the factors responsible for such change and we presume that it is fair to assume that the muscular hypertrophy of the medial coat is a compensatory change to provide for the additional strain on the smaller arteries of the vascular system from increased vascular tension. Criticism may be raised relative to the accuracy of readings of vascular studies on biopsy material but so long as the control also was made on biopsy material we believe that comparative reading is worthy of consideration and suggest that this thickening of the arterial wall is a definite finding associated with essential hypertension.

In grouping cases of hypertension according to the progress of the disease, Keith has called those with *slow* progression *benign hypertension*, those with moderate progression *early malignant* hypertension and those with rapid progression *malignant* hypertension since he hoped that these terms, benign early malignant, and malignant, would indicate not only the rate of progress, but would also signify the character of the symptoms for example that "malignant" would not only signify that the disease was rapid in its progress, but that the symptoms were also very marked. This classification is slightly misleading since the patients with benign hypertension in the later stages will present as marked cardiovascular and renal symptoms as those suffering from malignant hypertension However in order to have a better understanding of the progressive nature of the disease, it is well to follow this classification until a better one has been developed.

We, therefore, find that Keith's *benign* group those in which the disease develops *slowly* includes individuals in whom the disease originates between the ages of 40 and 55 years and continues for a period of 10 to 15 years before it develops to such an extent as to terminate life. In the earlier stages of benign hypertension intermittent headaches and the presence of retinal arterial spasm are the only symptoms and findings present other than that of elevated blood pressure.

Keith's second group *early malignant* hypertension, which develops *moderately fast* begins during that interval between the eighteenth and fiftieth years of life and progresses for a period of 3 to 4 years before death results. Retinal arterial spasm is associated with hemorrhages and evidence of retinitis. The blood pressure is capable of rises of 200 millimeters of mercury systolic and 160 millimeters diastolic. Irreparable cardiac, coronary and renal injuries present symptoms in the later stages of the disease in this group

Keith's third group, *malignant* hypertension, which progresses *rapidly* may occur during the same years as in the early malignant group However the life expectancy after the onset of symptoms in this group is much shorter and averages only 18 months. Examination of the fundus reveals arterial spasm, arterial sclerosis, retinitis, hemorrhage, and edema. The symptoms of cardiovascular and renal disease progress rapidly The systolic blood pressure frequently rises to 250 to 300 millimeters of mercury and the diastolic to 160 millimeters of mercury

REVIEW OF SURGICAL PROCEDURES

On the basis of postmortem investigations and theoretical considerations, section of the splanchnic nerves was suggested by Jean, in 1921 for the relief of pyloric spasm hyperacidity and hypersecretion. In 1923 Danielopolu considering the importance of the splanchnic nerves in the regulation of arterial pressure, conceived the idea of their resection in the treatment of hypertension. In the same

year Bruening and Stahl also suggested the same surgical procedure, and in 1924 Pende proposed, before the Congress of Internal Medicine at Milan, surgical treatment of arterial hypertension which consisted of resecting the left splanchnic nerves In 1927 Pieri (25) performed unilateral resection of the splanchnic nerves for intestinal atony In 1930 Pieri (26), following the suggestion of Pende, successfully resected the left splanchnic nerves of 2 patients who were suffering from arterial hypertension In 1932 Durante, of Genoa, resected the large and small left splanchnic nerves of 2 patients suffering from different arterial diseases These cases were reported by Santucci, and although they were not true cases of hypertension, the postoperative observation indicated a fall in both systolic and diastolic pressures In giving a résumé of the surgical techniques which have been described in the literature, Pereira stated that Pieri's technique consisted of resection of the splanchnic nerves by means of the supradiaphragmatic approach, after resection of the tenth, eleventh, and twelfth ribs Rossi attacked the splanchnic nerves between the attachments of the diaphragm after resection of the transverse process of the eleventh and twelfth thoracic vertebræ and, when necessary, the twelfth rib Pereira objected to the two previous techniques because of the danger of injuring the pleural sac, and he proposed section of the splanchnic nerves below the diaphragm without resection of bony structures

Our interest in attacking essential hypertension surgically began in 1925, when one of us (Adson), at the suggestion of Rowntree, performed bilateral lumbar sympathetic ganglionectomy and trunk resection, which included the second, third, and fourth lumbar ganglions on both sides, in a case of malignant hypertension There was some symptomatic relief, but the patient did not obtain a material drop in blood pressure and we doubt if this operation materially altered the progress of his disease The failure to lower the blood pressure, we believe, was due chiefly to the fact that the operation was limited in scope and did not include enough postganglionic rami to produce definite vasomotor relaxation During the same year, one of us (Adson) carried out unilateral cervicothoracic sympathetic ganglionectomy and trunk resection in a case in which a boy, 11 years old, had malignant hypertension His blood pressure had been very high and there was resulting cardiovascular damage Sympathectomy was performed for the purpose of determining whether or not it would produce vasodilatation of the retinal arteries as it does in cases of Raynaud's disease when spasm is responsible for the reduction in the caliber of the arteries In this case the disease had definitely produced sclerosis of the retinal arteries, and, consequently, no relaxation or increase in the caliber of the retinal arteries took place This discouraged us from proceeding with other operations on the sympathetic nervous system in this particular case, and it was not until 1930 that our interest was renewed by an experience one of us (Adson) had in which an attempt was made to relieve gastric crises due to syphilis by performing an extensive rhizotomy Rhizotomy in this last case consisted of section of dorsal and ventral roots on both sides, from the sixth thoracic to the second lumbar segments, inclusive The patient survived the operation, was able to get about, and was not materially inconvenienced by paralysis of the abdominal muscles, which condition was relieved by the aid of an abdominal supporter The pain of gastric crises was definitely relieved but, unfortunately, the patient succumbed several months later from general paresis

This experience, however, suggested the possibility that an extensive vasomotor paralysis might be accomplished by sectioning the anterior roots of both sides, from the sixth thoracic to the second lumbar, inclusive This was carried out by one of us (Adson) with the aid of Dr Craig The drops in blood pressure following successive sections of the ventral roots in the area described were phenomenal The systolic blood pressure dropped from 200 to 100 millimeters of mercury The diastolic blood pressure dropped from 120 to 90 millimeters of mercury, but, unfortunately, postoperative hemorrhage developed though the clot was removed and a partial spastic paraplegia developed which persisted These sequelæ prevented an immediate report of the

case and discontinuance of the operative procedure until October 10, 1933 when a second patient with essential hypertension was operated on At this time an extensive rhizotomy of the ventral roots on both sides, from the sixth thoracic to the second lumbar segments, was done. The revival of interest in the operation was prompted by two factors (1) The blood pressures of the original patient did not return to the pre-operative levels and the patient continued to survive the systolic blood pressure ranging from 140 to 160 millimeters of mercury and the diastolic from 80 to 110 millimeters and (2) the results of splanchnic section obtained by one of us (Craig) did not appear to produce the results desired, which suggested the possibility that the splanchnic operation as performed by him was not extensive enough in scope and did not include as many vasomotor fibers as did ventral root rhizotomy

One of us (Craig) has introduced an operation for essential hypertension which includes a section of the major and lesser splanchnic nerves below the diaphragm In addition, the sympathetic trunk between the twelfth thoracic and first lumbar sympathetic ganglions was divided This first operation was performed by Craig on October 26 1932 The approach used to expose the structures to be sectioned was a straight line incision placed laterally to the lower thoracic and upper lumbar spines on the left side. After the skin and subareolar tissues were reflected the latissimus dorsi and the quadratus lumborum muscles were incised The approach gave excellent exposure of the splanchnic nerves but was inadequate to permit removal of the two upper sympathetic ganglia However in subsequent cases, Craig did include the first lumbar ganglion with section or resection of the splanchnic nerve On April 1 1933 Craig employed the supradiaphragmatic approach in 1 case for section of the major and lesser splanchnic nerves. He entered the mediastinum on the right side opposite the eleventh rib after having resected 4 centimeters of the rib adjacent to the transverse process in order to secure exposure of the splanchnic trunk The pleura was rather thin, and it was opened during the operation Consequently he chose to employ the subdiaphragmatic technique previously referred to for his future resection of splanchnic nerves and removals of first lumbar ganglia.

Perhaps the same comment might be applied to these procedures as was applied to those used by Peet, and which justify the modification as proposed and carried out by one of us (Adson) This new approach is a subdiaphragmatic, intra-abdominal, retroperitoneal approach through a high kidney incision. It permits of ample room and exposure of the splanchnic nerves, first and second lumbar ganglia, and the suprarenal gland It appears that the result is as effective a vasodilating procedure as extensive bilateral ventral rhizotomy

Up to the present, October 1 1935, 27 patients with essential hypertension, of varying degrees of severity and progress, have been submitted to extensive rhizotomy Seven have had bilateral section of splanchnic nerves including the major minor and lesser splanchnic nerves. Seven patients have been subjected to bilateral resection of splanchnic nerves with removal of the first and second lumbar sympathetic ganglia on both sides. Specimens for biopsy were taken from each suprarenal gland in 1 case and resection of half the suprarenal gland on each side was performed in the 6 other cases Four patients have been operated on for essential hypertension by miscellaneous procedures, namely bilateral lumbar sympathectomy left cervicothoracic sympathectomy resection of the sixth to the twelfth intercostal nerves to produce paralysis of abdominal muscles, and complete removal of one suprarenal gland and removal of three-fifths of the opposite suprarenal gland, performed by Walters (19) and his associates.

Crile for a number of years has attempted to alter the cycle of endocrine secretions, chiefly those of the suprarenal gland, and has performed numerous denervations for a variety of cyclo-asthenia as well as for recurring hyperthyroidism, recurring duodenal ulcer vasomotor disturbances, and hypertension. Denervation itself has apparently not controlled essential hypertension, but when combined with splanchnic section it has been

quite effective The DeCourcys (11, 12) have followed the line of reasoning of certain physiological investigators who believe that the amounts of epinephrine secreted are the factors responsible in determining the course of hypertension They have, therefore advised and performed resections of the suprarenal glands, believing that it is necessary to resect from three-fourths to four-fifths of each gland in order to produce the desired drop in blood pressure, and that it is possible to resect such quantities of the suprarenal gland without producing glandular deficiencies and Addison's disease Page and Heuer have reported a goodly series of cases of hypertension in which treatment has been by ventral root rhizotomy Rhizotomy has varied from complete inclusion of roots from the sixth thoracic to the second lumbar, to partial rhizotomy, taking either the upper or lower half of the group described Their results are not unlike ours, unless perhaps they are slightly better, which might be explained on the basis that they made better selections of cases for operation, whereas in the beginning we had to select our cases more or less by trial and error

Peet recently reported, at the Surgical Section of the American Medical Association, a large series of cases in which he had sectioned the splanchnic nerves on each side He entered the mediastinal cavity on each side of the spinal column after resecting a portion of the eleventh rib on each side He then proceeded to section the major splanchnic nerves opposite the ninth thoracic vertebra and the lesser splanchnic nerves opposite the eleventh thoracic vertebra His results are unusually good, and he attributes them to the fact that section of the splanchnic nerves above the diaphragm interrupts a few postganglionic rami which travel along the abdominal aorta to join the celiac plexus Even though this is true, the white rami carrying vasomotor fibers, as well as fibers of suprarenal innervation, cannot be included in the operation as performed by him above the diaphragm Furthermore, if this were true, the extensive rhizotomy which includes the ventral roots of the sixth thoracic to second lumbar vertebræ should be as effective, if not more so, since it interrupts all of the preganglionic thoracolumbar sympathetic fibers below the fifth thoracic segment There is a possibility that section of postganglionic rami may be more effective in relieving vasomotor spasm than section of preganglionic fibers

Extensive rhizotomy, whether performed in one or two stages, is a rather formidable procedure It was for this reason that one of us (Adson) therefore proposed, and carried out first on February 11, 1935, a subdiaphragmatic exploration of the splanchnic nerves, the first and second lumbar ganglia, and the suprarenal gland Through the right and left explorations, respectively, all of the splanchnic nerves as they enter the abdominal cavity and the first and second lumbar sympathetic ganglia can be resected, thus interrupting the white rami which carry efferent impulses to these ganglia and lumbar trunks to the celiac and renal sympathetic ganglia One is also able to explore, to take specimens for biopsy, or to resect, the suprarenal gland

Up to the present time 7 patients have been operated on by this procedure, without fatalities Six of them have undergone operations on the right and left sides, respectively, on separate dates, with intervals of 10 days to 3 months between operations The results of these various operations will be evaluated in another paragraph and so it is sufficient to say here that it appears that the results obtained from a combination of resection of splanchnic nerves and removal of the two upper lumbar sympathetic ganglions, in conjunction with resection of the suprarenal gland, is as effective as extensive rhizotomy, if not more so, since there is an opportunity to resect the suprarenal gland without producing trauma to the remaining portion

BLOOD PRESSURE REACTIONS IN HYPERTENSION

The underlying and primary abnormality demonstrated in cases of essential hypertension has been an excessive response of the blood pressure to various forms of stimulation This response is of the same order as that observed in non-hypertensive subjects, but it is excessive The work of Hines and Brown on the hereditary factors indicates that this excessive reaction occurs early in life and follows the laws of heredity The modern

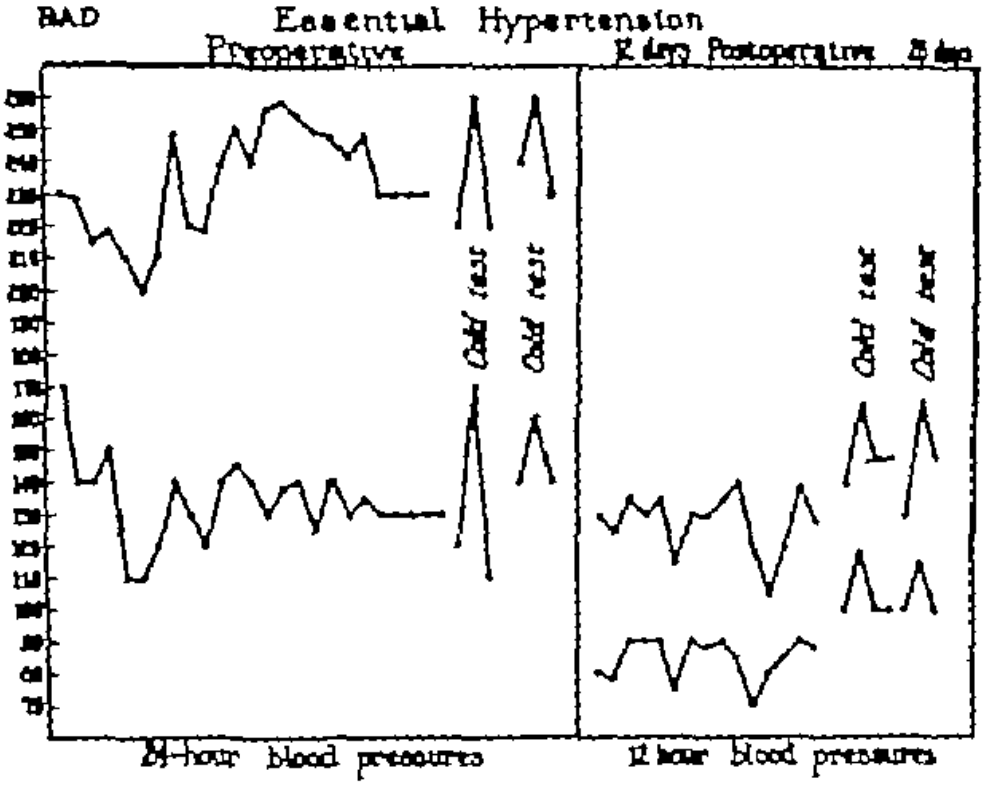

Fig. 1 Variations in systolic and diastolic blood pressures prior to rhizotomy. The two interrupted lines of the cold tests taken before rhizotomy illustrate the height that both the systolic and diastolic pressures may attain. The chart on the right represents similar readings taken following rhizotomy

conception of essential hypertension is, then, that the individual inherits a hypersensitive vasomotor mechanism, as measured by the blood pressure. This excessive reaction may be a causal factor in the production of hyper tonus and hypertrophy of the arterioles, which eventuates in increased levels of blood pressure and in what we recognize as the clinical stage of essential hypertension

A simple method has been evolved to measure the reactibility of the blood pressure. This has been designated as the *cold pressor test* (Fig 1) and consists of placing the patient s hand in ice water at 4 degrees C and taking the blood pressure. The basal blood pressure is obtained during rest the hand is then placed in the ice water and in 30 seconds the blood pressure rises to what is known as the *ceiling* or highest response. The blood pressure returns to normal in from 2 to 8 minutes. This pressor test then becomes a measure of the individual s response to a given stimulus. It is constant for the hypertensive or prehypertensive individual and is three to ten times greater than that found in the normal or non-hypertensive subject. The application of this test is important in the evaluation of the effects of therapeutic procedures. Measures to control the blood pressure, to be effective, must control this variability factor Surgical measures in which the vasomotor control of a large portion of the blood vessels is cut off from the central mechanism can be evaluated to an accurate degree by the change and reduction of the ceiling and vasomotor response to the cold pressor test. It becomes an effective measuring rod for therapeutic procedures. It obviates in some degree the difficulty encountered by attempting to evaluate therapeutic measures in hypertension by occasional readings of the blood pressure.

STUDIES ON THE EFFECT OF POSTURE ON BLOOD PRESSURE

The completeness of surgical procedures which denervate the splanchnic circulation can be measured with considerable accuracy by studying the effects of posture on blood pressure. The blood pressure normally changes to some degree with changes in pos-

ture In persons suffering with the clinical syndrome known as postural or orthostatic hypotension (Fig 2) there is a drop in the blood pressure, both systolic and diastolic, while the patient is in the upright position which is sufficient to produce syncope Associated with these drops is, in addition loss of sweating in certain areas of the body Following extensive anterior rhizotomy, a fall in blood pressure develops which is comparable to that seen in postural hypotension This is measured by placing the patient on a table which can be tilted at various angles The blood pressure is taken with the patient in the horizontal position, then with the head down and the feet up, and then with the head up and the feet down A drop of from 40 to 80 millimeters of mercury in the systolic blood pressure with an increase in the pulse rate has been observed with the patient in the upright position A drop of this magnitude presents objective evidence of the loss of splanchnic control to maintain the blood pressure in the upright position Lesser degrees of drop in blood pressure have been observed after the less extensive operations

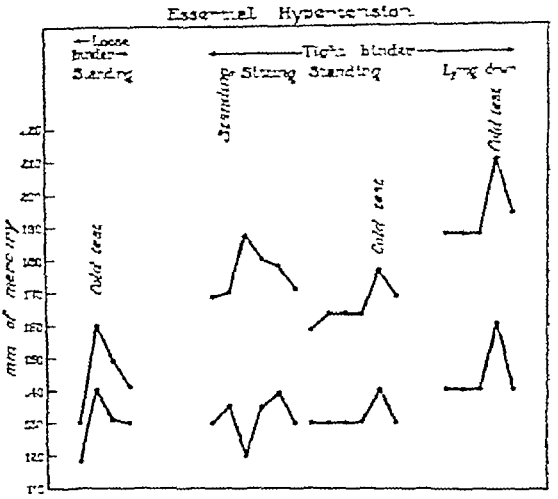

Fig 2 Variations in blood pressure following rhizotomy, while patient is standing or lying down, and the reactions to the cold test with or without the abdominal binder Rhizotomy produces a hypotension which can be regulated by the application of an abdominal support.

pressor test ' the age of the patient, and the amount of cardiovascular and nephritic damage present Our experience with patients submitted to the various types of sympathectomy and rhizotomy has taught us that the best results will be obtained when symptoms are still mild and when there is definite evidence of an unstable level of blood pressure that is when the least excitement or continued exertion results in systolic peaks of 200 millimeters or more and diastolic peaks of 120 to 160 millimeters

Naturally one does not want to advocate surgical intervention in the treatment of this disease unless there has been definite evidence that one is dealing with essential hypertension On the other hand it is useless to advocate sympathectomy when the high levels have become sustained and when irreparable damage has resulted from the progress of the disease We are quite convinced that when medical measures fail and when the cold pressor tests reveal hyperactive responses as observed in essential hypertension surgery is indicated Our experience also reveals that patients developing symptoms in the third and fourth decades of life respond most favorably to surgical intervention and that those presenting the symptoms, as grouped by

RENAL FUNCTION

Studies on renal function have shown that there is a definite change in the excretion of water with the various postures after section of anterior roots In daytime, when the patient is in the upright position, there is a decrease in the excretion of water, during the night with the patient in a recumbent position and when there is a higher blood pressure there is an increased excretion of water and nocturnal polyuria Page and Heuer in the report of a case have shown that urinary efficiency and the ability of the kidneys to concentrate was normal before this operation and remained unchanged afterward

SURGICAL INDICATIONS AND SELECTION OF CASES

In attempting to select cases which will respond to rhizotomy or extensive sympathectomy, it is necessary to take into consideration the character of the symptoms the rate of progression of the disease the response to medical measures, the effects of the "cold

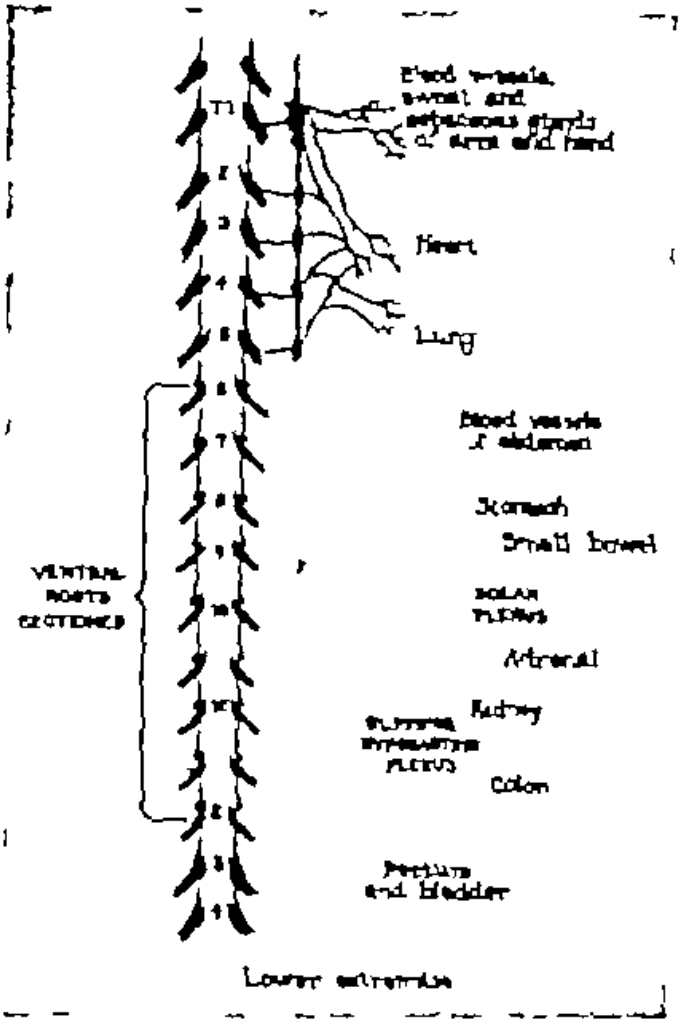

Fig 3 Sympathetic nervous system affected by sectioning ventral roots for essential hypertension from sixth thoracic to the second lumbar segments on both sides The sympathetic ganglions shaded dark represent those which receive efferent impulses, and those that are left light have been deprived of these impulses

Keith in the benign hypertensive group and the early malignant hypertensive group will obtain much more satisfactory results than will those who are grouped within the malignant group since those in the first two groups will still have an elastic vascular system capable of being relaxed whereas in the latter group there is more likely to have been permanent damage with arteriosclerosis and fixation of the vascular walls This latter group is unable to respond to vasodilating measures, and the condition invariably has resulted in irreparable damage to the vascular system heart and kidneys.

We are quite in accord with the practice of having every patient who submits himself or herself for examination for hypertension carefully analyzed and the status of the disease determined before active surgical treatment is instituted. Although there is no specific medication or diet for the treatment of this disease a therapeutic test of the medical regimen is worth while to determine whether or not it is possible to decrease the blood pressure and to ameliorate the symptoms The usual advice given consists in encouraging the patient to live less strenuously to regulate hours of work, with daily midday rest periods of an hour and to adjust his program in order to reduce the worry associated with economic or social existence. Avoidance of overweight a change of vocation or an extended vacation—all are of definite value in attempting to reduce a strenuous existence. In the more extreme cases, continued rest in bed and the administration of such barbiturates as phenobarbital and sodium amytal may temporarily lower the blood pressure and reduce the intensity of the symptoms.

In an attempt to select suitable cases for operation in the beginning of this study patients were subjected to spinal anesthesia for the purpose of determining if the drops in blood pressure could be affected by temporarily paralyzing the functions carried over the ventral roots below the fifth thoracic segment. Curiously enough blood pressures dropped in all cases, regardless of the phase of the disease. Much of the drop may have been due to an extensive vasomotor paralysis, which included all the vessels below the diaphragm. There was also a possibility however that the spinal anesthetic produced part of this drop in blood pressure by inhibiting the central mechanism through the absorption of the anesthetic. The test of spinal anesthesia is, therefore not as reliable as one would wish in the selection of suitable cases for operation.

SURGICAL TECHNIQUE

The two operative procedures which we have employed consist of (1) extensive bilateral section of ventral roots of the lower thoracic and upper lumbar roots, and (2) extensive subdiaphragmatic sympathectomy which includes the splanchnic nerves on each side as well as the two upper lumbar ganglia, and

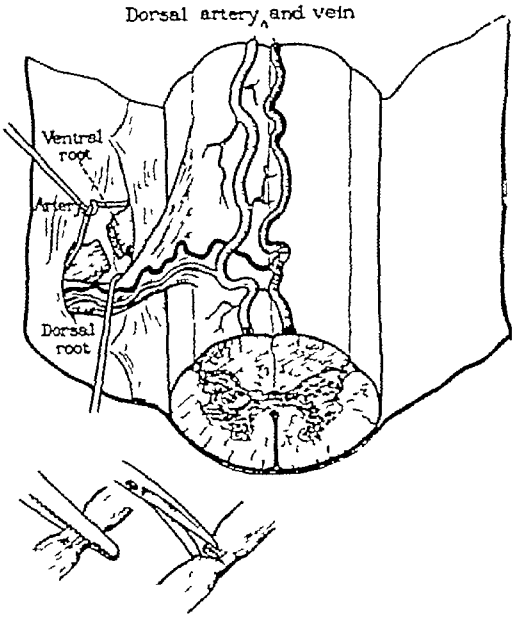

Fig 4. Showing the technique employed in sectioning a ventral root while the arteries and veins about it are preserved.

biopsy or partial resection of the suprarenal gland *Rhizotomy* has been used more often than splanchnic operation, since it is larger in scope and it would appear that more vasomotor impulses would be interrupted by that operative procedure than would be by the latter operation However, inasmuch as rhizotomy is a formidable procedure, we have been interested in devising ways to reduce the surgical shock, but still produce as effective vasodilatation One of us (Adson) therefore was prompted to devise a subdiaphragmatic technique of splanchnic resection with a lumbar sympathectomy

The indications for the selection of cases and pre-operative preparation are the same for either operation However, both procedures are being employed, not necessarily on alternate cases, but on similar cases in the various phases of the disease in order that we may evaluate the results from each procedure until one operative measure has shown results that definitely supersede those of the other Once having selected the patient for operation, he or she should be permitted to quiet down thoroughly from the effect of the numerous

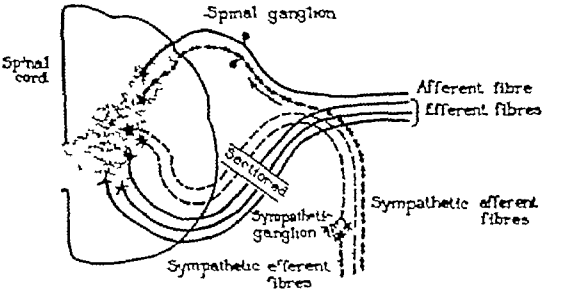

Fig 5 Section of ventral root to interrupt preganglionic rami

examinations before being submitted to operation It may even be wise to administer small doses of amytal for 2 or 3 days and to give a dose of 3 grains (0 20 gram) of pentobarbital sodium on the morning of the operation 1 hour prior to transfer to the operating room It has been observed that drop ether anesthesia, administered over an inserted intratracheal Magill tube, is as safe and satisfactory an anesthetic as we have employed If no sudden and extreme rises or falls in blood pressure develop during the operation, we prefer to complete the rhizotomy in one stage

RHIZOTOMY

On reflection of the dura, following the laminectomy, it is very important to avoid injury to the small arteries or veins accompanying each pair of roots Those adherent to the ventral roots should be dissected free with delicate hooks After these vessels have been separated from the ventral roots, it is not necessary either to ligate the root or to clip it with a silver clip, since the capillaries within the root between the fasciculi are readily crushed by compression of the root with a Kelly forceps preliminary to their division with a sharp scissors (Figs 3, 4, and 5) The reason for protecting this blood supply is to assure the dorsal and ventral arteries and veins of the cord their collateral circulation It is true that these communicating arteries and veins are not very large, but one of us (Adson) observed that a disregard for these vessels in performing ventral rhizotomy in one case resulted in permanent urinary retention It is needless to urge hemostasis, for the experience of one of us (Adson), obtained in his first case, more

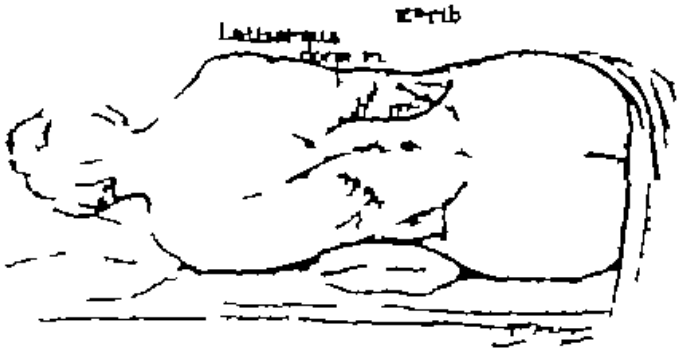

Fig 6 Approach to the extraperitoneal subdiaphragmatic space in order to resect the splanchnic nerves, to remove the first and second lumbar ganglia, and t resect the suprarenal gland, for essential hypertension

than emphasizes the importance that extraordinary precautions regarding hemostasis are necessary when laminectomy of such magnitude is undertaken.

One of us (Brown) has urged limitation of the extent of rhizotomy and both Craig and Adson have employed modifications of the original procedure in that in some instances, the bilateral ventral roots have been divided only from the sixth to the ninth thoracic segments. In other cases the roots have been divided from the tenth thoracic to the second lumbar segments, and in still other cases patients who underwent this partial rhizotomy have been submitted to the second stage, which included completion of the division of the remaining ventral roots carrying sympathetic impulses over the lower two-thirds of the thoracolumbar outflow Postoperative observations and studies have shown rather conclusively that complete rhizotomy has been more effective than the limited one Page and Heuer have made a very good suggestion recommending that if the operation is to be divided into two stages that it be divided at the completion of laminectomy before the dura is opened thus, at the second stage of the operation, the time-consuming procedure of laminectomy is obviated and one can almost instantly proceed with section of the ventral roots.

EXTENSIVE SYMPATHECTOMY

The incision employed (Fig 6) and the position of the patient on the operating table for extensive sympathectomy are similar to those employed for exploration of the kidney except that the incision is made to follow anatomical lines. The line of the incision is similar to that of a hockey stick, with a staff portion placed just lateral to the rectus spinous muscles and the *club portion extending* obliquely downward and forward over Petit s triangle just above the crest of the ilium At the upper portion of the wound after the skin and subareolar tissue have been incised the oblique fibers of the latissimus dorsi muscle are incised thus exposing the twelfth rib As the incision is extended downward along the course of the skin incision the common aponeurosis of the external and internal oblique muscles, and of the transversalis muscle where it fuses with the lateral reflection of the lumbar fascia, is incised until the fusion extends into Petit s triangle, exposing the capsule surrounding the perinephritic fat.

The next step in the operation consists of performing subperiosteal resection of the twelfth rib (Fig 7) care being taken not to injure the pleura the finger is then introduced into the subdiaphragmatic space above the perinephritic fat in order to dissect free the subcostal ligament of the twelfth rib since division of this will allow upward retraction of the structures, periosteum of the twelfth rib intercostal vessels, and nerves, which affords a much better exposure of the splanchnic nerves and lumbar ganglions A wide illuminated retractor is then introduced into the wound at right angles to the spinal column It is used to displace the liver forward and downward and at the same time to lift the capsule about the perinephritic fat with its contents (the kidney and suprarenal gland) in a similar direction Since the patient is placed on his side with elevation of the opposite loin with the kidney rest, it is not difficult to displace these structures forward and downward care always being taken to avoid sudden or jerking movements The tissues are further protected by introduction of a salt laparotomy sponge with the retractor placed on the sponge to assure against trauma to the underlying tissues. Gentle dissection with moist cotton ball sponges reveals, first, the splanchnic trunk composed of major and minor and lesser splanchnic nerves which are about 2 centimeters in length Dissection is carried medially until the lateral border of the celiac

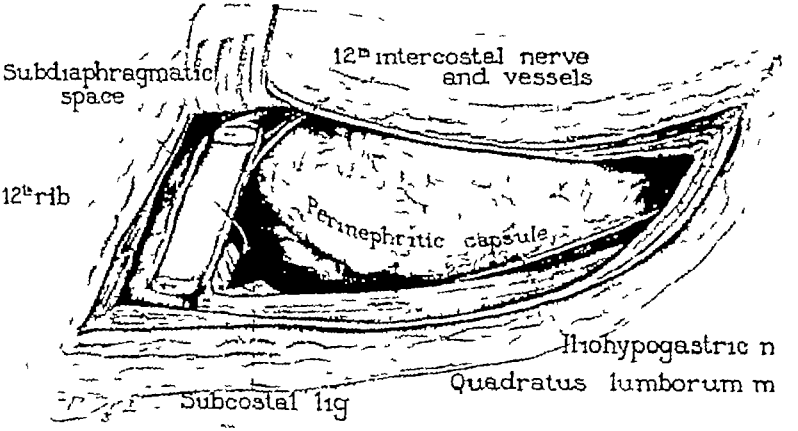

Fig 7 Resection of the twelfth rib, with elevation of perinephritic fat and capsule, and division of the subcostal ligament, exposing the retroperitoneal subdiaphragmatic space

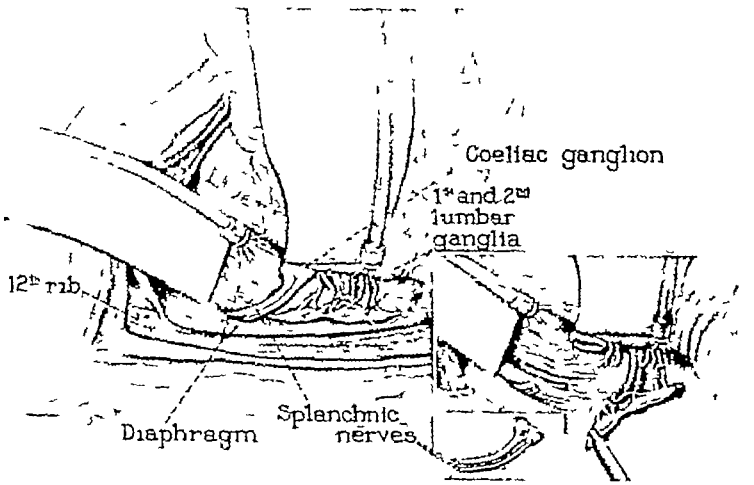

Fig 8 Exposure and resection of splanchnic nerves, with a portion of the celiac ganglion, and removal of the first and second lumbar ganglia

ganglion is exposed The resection includes a few millimeters of the ganglion with the splanchnic nerves (Fig 8) The first and second lumbar sympathetic ganglia are exposed in turn and are removed in conjunction with the intervening trunk in order to interrupt fibers that pass downward in the lower end of the thoracic sympathetic trunk as well as to interrupt white rami carrying efferent impulses to the upper two sympathetic lumbar ganglia

After hemostasis has been thoroughly controlled, the liver and perinephritic fat capsule are allowed to fall into place before the perinephritic fat capsule is incised over the upper pole of the kidney A Halsted forceps is then placed on the renal capsule just superficial to the peripheral border of the suprarenal gland (Fig 9) Gentle retraction on the forceps elevates the upper pole of the kidney, and presents the suprarenal gland into the field The gland is now so superficial that one can readily explore it, and resect any portion of the gland desired, without injury to the remaining portion In light of the work of Crile and DeCourcy, one of us (Adson) has resected the

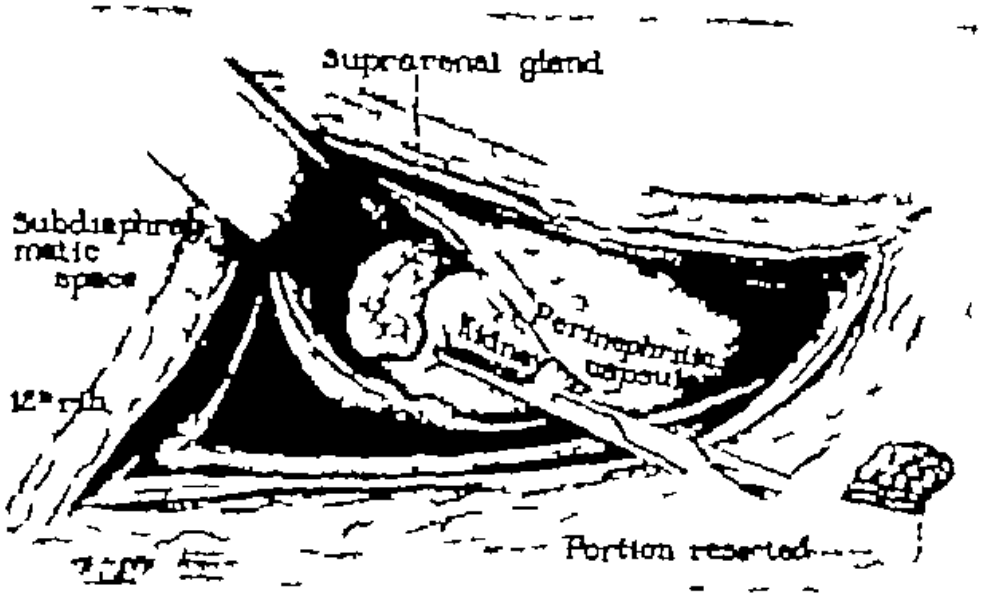

Fig 9 Elevation of superior pole of kidney, with exposure of suprarenal gland, employing the same incision used for splanchnic resection and removal of lumbar ganglia

outer half of the gland on each side in 6 cases in conjunction with splanchnic nerve resection and removal of lumbar ganglia. In doing so the outer portion of the gland is elevated from the kidney without injury to the blood vessels, since most of these enter the gland from the medial and dependent portion of it. Two stick ties of double No 00 catgut are introduced into the middle of the gland ligating *first to one side and then to the other* The outer or distal portion of the gland can then be *removed without hemorrhage or trauma to* the remaining portion. The perinephritic fat capsule is closed with interrupted sutures of catgut and dropped into place. The kidney rest is then lowered the muscular fascial planes are approximated with continuous and interrupted sutures of No 1 chromic catgut (Fig 10) The subareolar tissue is approximated with continuous No 1 plain catgut. The skin is closed with interrupted silkworm sutures and approximated with a continuous locking stitch of dermal or silk sutures. No drainage is employed.

Postoperative care corresponds in the one instance to that which is employed in the *treatment of patients who have undergone* laminectomy for lesions of the spinal cord whereas in the other instance it is similar to that which is employed in the treatment of patients who have had operations on the kidney or upon the suprarenal gland

ANALYSIS OF RESULTS FOLLOWING OPERATION

The purpose of the operation is to destroy the vasomotor innervation to a large vascular area (Fig 11) in order that those vessels which are deprived of their vasoconstrictor impulses will be unable to respond to the central mechanism and *therefore be unable to take part* in the general phenomena of vasospasm While the vessels which have not been denervated continue with spasm the denervated vessels dilate instead and act as reservoirs It must not be forgotten however that the musculature of the heart and blood vessels is capable of responding directly to the pressor and depressor substances circulating in the blood stream, and that there is a possibility that these substances increase, or that the musculature becomes more active, as a compensatory factor following these extensive forms of sympathectomy It is, therefore, further possible that this is the explanation for the surgical failures.

Operative procedures on the suprarenal gland suggest that a diminution of the secretion of epinephrine is a beneficial factor in the treatment of the disease. The evidence to date, however is not conclusive or indisputable

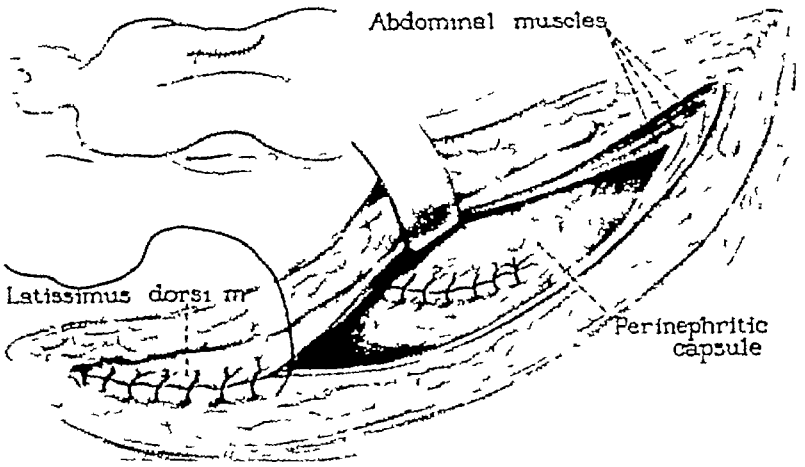

Fig 10 Closure of wound in anatomical planes

POSTOPERATIVE CLINICAL OBSERVATIONS

Promptly following one of these extensive operations the systolic blood pressure is capable of dropping from 270 millimeters or more to a reading of 100 millimeters of mercury, and the diastolic is capable of dropping from 170 millimeters down to 60 millimeters of mercury The same observations have been found following either rhizotomy (Fig 12) or splanchnic (Fig 13) resection As long as the patient remains in bed, these pressures remain low and the systolic pressure may not rise above 140 and diastolic not above 90 millimeters, as the patient gets up and about however the systolic pressure may rise to 160 or 170 millimeters and the diastolic to 90 to 110 millimeters The most significant observation is that the sudden and abrupt peaks of blood pressure will not occur following operation as they did prior to operation The variability in both the systolic and diastolic pressures, and the mean pressures of both, have been materially reduced A review of our series of rhizotomies shows the mean systolic drop to be 44 millimeters and the mean diastolic drop 38 millimeters of mercury Improvement in clinical symptoms is probably more manifest than the actual drop in blood pressure, since these patients very promptly inform us that their throbbing headache, cardiac consciousness, and precordial distress disappear The ocular symptoms as well are markedly im-

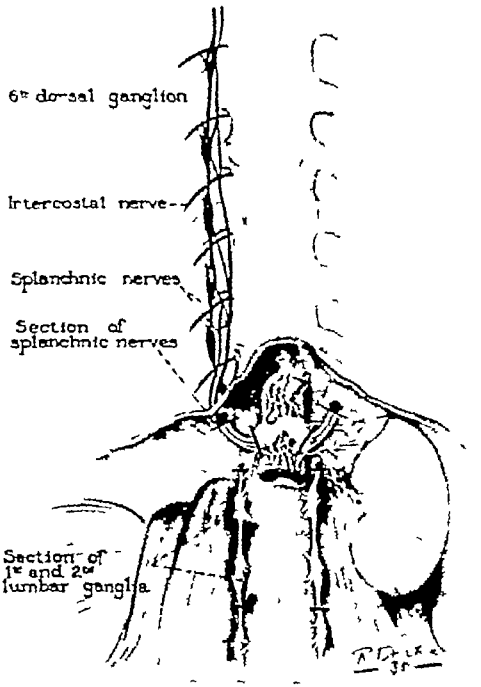

Fig 11 Schematic drawing showing the splanchnic nerves and celiac and lumbar ganglia and as well the lines of resection and the effects which are produced when the splanchnic nerves are resected and the first and second lumbar ganglia are removed on each side The sympathetic ganglia which have been shaded dark represent those which receive efferent impulses, and those that have been left light have been deprived of these impulses

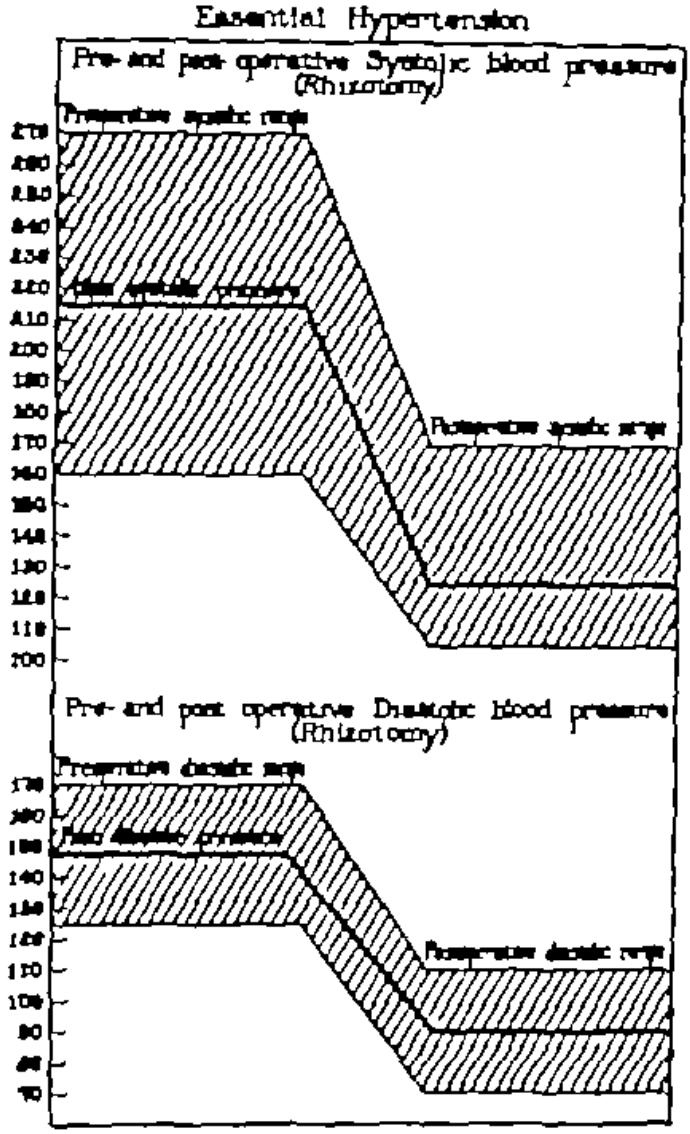

Fig A typical case of essential hypertension, showing the range of systolic and diastolic blood pressures taken over 24 hour periods before and after extensive rhizotomy The postoperative readings represent the decrease in blood pressures, with a decrease in the range of systolic and diastolic blood pressures, recorded after a postoperative interval of four weeks

proved. Spasm of the retinal artery is less, a phenomenon *which is difficult to understand* since these vessels have not been denervated by either the rhizotomy or splanchnic resection. It would thus appear that part of the spasm is a defense mechanism to protect against rupture but which also works in a vicious circle to contribute to the phenomena of vasospasm and hypertension The reduction of blood pressure seems to diminish the reflex stimulus, which accounts for some of the relaxation of the vessels as observed by studies of the retinal arteries in the various phases of the disease and its treatment. Retinal hemorrhages and papilledema will often disappear following sympathectomy If the damage to the kidneys or heart or brain has not been too extensive a moderate degree of improvement may be anticipated

Laboratory studies reveal that there is a definite water lag during the day when the blood pressures are lower than during the night when the patient is in a reclining position A moderate polyuria at night may appear to compensate for the deficient excretion during the day Excretion of dye is not influenced by low pressures. There has been no change in the sugar tolerance and also no change in the creatinine or serum sulphates Patients with renal damage presented high values for urea immediately after operation a condition which corrected itself by the time of dismissal 4 weeks after operation. The cold pressor tests following operation produce lower levels with smaller variables, following operation than they did before it. Readings of blood pressure in the various positions, such as the erect reclining and Trendelenburg position reveal definite evidence of hypotension a situation that occurs frequently following extensive rhizotomy and has occurred following extensive splanchnic resections The systolic blood pressure is capable of dropping to such an extent that, when the patient is standing in the upright position syncope occurs but fortunately it can be corrected by applying an abdominal supporter and adjusting the tension.

The results of the various operations have been compiled in chart form in an attempt to evaluate the accomplishments of the various operative measures (Table I) The groups for each operation have included about an equal distribution of benign, early malignant and malignant hypertensions Two deaths have occurred one resulting from hemolytic streptococcal meningitis, and the other from a ganglioneuroma with advanced cardiorenal degeneration In this last case death probably was due to cardiac failure, as it occurred very suddenly after the patient had recovered from the anesthetic The patient s blood pressure rose to 300 millimeters of mercury systolic at the first attempt at rhizotomy and operation

TABLE I—RESULTS OF VARIOUS SURGICAL PROCEDURES FOR ESSENTIAL HYPERTENSION—1935

Type of operation	Cases	Results			
		Good	Fair	Failures	Deaths
Extensive rhizotomy	27	13	6	6	2
Splanchnic section with removal of first lumbar ganglion	7	2	1	4	0
Splanchnic section with removal of first and second lumbar ganglia and partial section of suprarenal gland*	7	5	2 (one side)	0	0
Miscellaneous	4			4	0
Total	45	20	9	14	2

Average systolic drop 44 mm of mercury
Average diastolic drop 38 mm. of mercury

*Ten additional patients have been operated upon
No deaths, results very satisfactory Suggests that this operation is the one of choice.

was therefore postponed without making an incision At the second attempt, even though the patient was "saturated" with pentobarbital sodium, it again rose above 270 millimeters systolic. Following completion of the operation, the blood pressure had dropped to 90 and 50 millimeters of mercury, respectively The four miscellaneous operations, as previously stated, included limited procedures to determine what influence they might exert on lowering the blood pressure We have previously commented on the effects of lumbar sympathectomy and unilateral cervicothoracic sympathectomy Division of the intercostal nerves, from the sixth to the eleventh roots on both sides in the postaxillary line, produced paralysis of the abdominal muscles with a drop of systolic pressure of 10 to 20 millimeters of mercury, a drop in blood pressure of no significance The fourth case, in which the suprarenal glands were resected without inclusion of sympathetic nerves, will undoubtedly be reported later by Walters The results, as far as influencing blood pressure are concerned, are rather disappointing

SEQUELÆ FOLLOWING RHIZOTOMY AND EXTENSIVE SPLANCHNIC SECTION

Following complete rhizotomy, there is loss of the sweating function of the feet, legs, and lower part of the abdomen up to a transverse

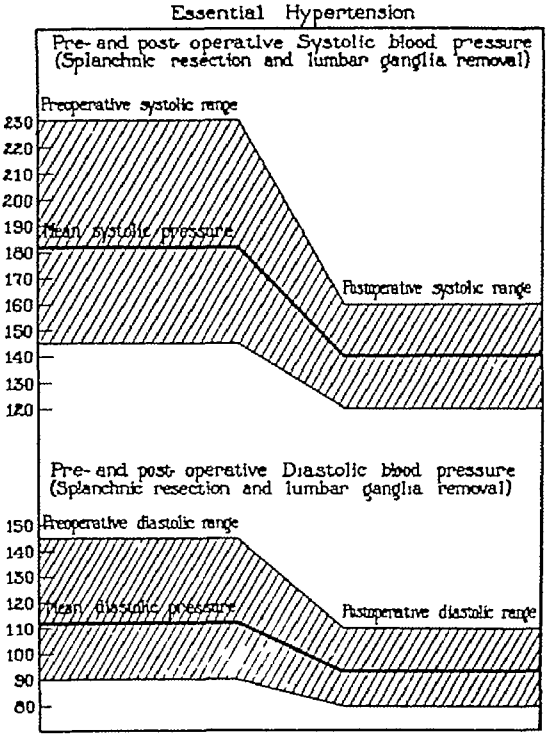

Fig 13 A typical case of essential hypertension, showing the range of systolic and diastolic blood pressures taken over 24 hour periods before and after bilateral splanchnic resection, bilateral removal of first and second lumbar ganglia, and bilateral resection of suprarenal glands The postoperative readings represent the decrease in blood pressures, with a decrease in the range of systolic and diastolic blood pressures, recorded after a postoperative interval of 4 weeks

line situated about 1 to 2 inches (2 5 to 5 centimeters) above the umbilicus The skin is slightly pinker than normal in appearance and is definitely warmer, thus producing the same vasomotor phenomenon that follows bilateral lumbar sympathectomy There is a paralysis of ejaculatory powers and muscles of the urogenital trigone similar to that following neurectomy of the presacral nerves This phenomenon does not alter the menstrual cycle or does it disturb the child-bearing functions in the female, but it does result in sterility of the male although it fortunately does not disturb the potentia or the libido Though rhizotomy deprives the small and large bowels and the bladder of their sympathetic innervation, it does not appear to increase the frequency of urinary or fecal evacuation.

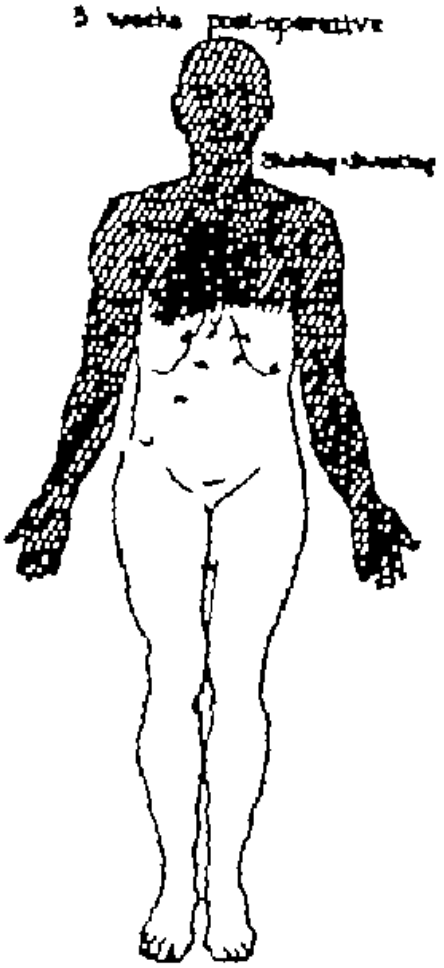

Fig 14 Areas of skin in which the sweating function has been abolished by an extensive rhizotomy for essential hypertension The operation included bilaterally the ventral roots from the sixth thoracic to the second lumbar segments

The effects of splanchnic resection and removal of the first and second lumbar ganglia are similar to those obtained by rhizotomy except that the level of sweating and sebaceous loss and increase in surface temperature occurs at a lower level than that observed in rhizotomy (Fig 14) Since the level in this latter group corresponds to the first lumbar segment this loss of sweat secretion and the vasomotor relaxation continues downward from this level to include the feet. Though it appears that the autonomic nervous system and particularly the sympathetic nervous system plays an important rôle, according to Cannon, in the regulation of the homeostasis of the human body it is possible for human beings as well as experimental animals to live without its influence, in limited areas at least

SUMMARY AND CONCLUSIONS

Analysis of the data following surgery indicates that certain definite results have been obtained by these extensive operative procedures. However it also shows that a limited number of patients fail to respond to the same procedure, while still others have obtained clinical improvement without a material drop in blood pressure some of them having had a return of their old symptoms and of their high blood pressures. The interval following these surgical procedures is too short to prognosticate what the ultimate results will be One of our patients has now survived for approximately 5 years, but the remaining group have survived 25 months or less. The immediate effects in many cases have justified the surgical treatment, and they have encouraged us to continue with the operative measures in the hope that better selection of cases may be made and that subdiaphragmatic splanchnic resections with removal of the upper two lumbar ganglia and resection of the suprarenal gland may be more effective in controlling or relieving symptoms of essential hypertension than the operation of bilateral ventral rhizotomy of the thoracic and lumbar roots extending from the sixth thoracic to the second lumbar inclusive.

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THE MEDICAL PROBLEM AND MANAGEMENT IN ESSENTIAL HYPERTENSION[1]

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THE history of the early attempts to read the secrets of the pulse the circulation, and the pressures within the vessels would provide an interesting chapter Read the delightful account by Brim running from Herophilus and Galileo through Harvey Hales Poiseuille to Herisson the last named, the first to invent a blood pressure apparatus to measure the blood pressure in man. From there his account carries on from von Basch who is said to have made the first actual scientific blood pressure measurements in man, to Riva Rocci, to whom we owe the prototype of the sphygmomanometer in widest clinical use today On the way we meet Frederick Akbar Mahomed in Guy's Hospital, from whose paper On Albuminuria" in 1883 Brim quotes Lastly I may point out that I have demonstrated that the increase of arterial pressure precedes the appearance of any symptoms of renal disease." This terse sentence is expressive of Mahomed s discovery of the pre-albuminuric stage of hypertension.

The similarity in the histological changes found in the kidney when sclerosis of the renal arterioles causes closure and consequent atrophy of the glomerular capillaries and in the changes seen in chronic glomerulonephritis has long caused confusion in our ideas as to etiology and consequently in our methods of management as well It has taken the greater part of the century since the publication of Bright's classical work in 1827 to clear away the confusion these similarities have brought about. This is being accomplished by the slow and painstaking processes of investigation by innumerable workers in the clinic and laboratory in chemistry and in physiology

In recent years much of the confusion between the histological picture in chronic glomerulonephritis and that in essential hypertension is cleared up by recognition of the fact that in the latter the arteriolar lesions precede the lesions in the glomerulus In describing the arteriolosclerosis kidney Bell states that as the lumen of the arteriole becomes narrowed, the glomerular capillaries collapse and the basement membrane increases until the entire glomerulus assumes a compact hyaline appearance. The closure of the glomerular capillaries brings about a disuse atrophy of the associated tubule. Closure of small arteries causes atrophy of groups of glomeruli and their tubules. When a sufficient number of tubules have atrophied, the cortex shrinks and the surface of the kidney becomes pitted. Renal insufficiency develops when the atrophy becomes pronounced. Sclerosis of small arteries is as important as arteriolosclerosis in causing atrophy and renal insufficiency

Further the development of uremia in essential hypertension during the stage to which Fahr gave the name "malignant hypertension" serves to emphasize the toxic and degenerative features and to make most investigators give consideration to the idea that there must be some toxin responsible for the retrogressive changes both in the arterioles and in the small and large arteries Probably the most outstanding recent work expressive of this search for some specific toxic substance causing hypertension is that of Major who demonstrated in animals prolonged elevation of blood pressure following injection of guanidine. He found guanidine present in the blood in increased amount in 15 cases of chronic nephritis, in 13 of which there was a coincidental retention of nitrogen. He found also increased guanidine in the blood in 61 per cent of his patients with essential hypertension but did not differentiate between the simple, benign and 'malignant" forms. The search for a pressor substance in nephritis and renal toxemias does not concern us here.

A differentiation between the vascular changes in decrescent arteriosclerosis and those changes occurring in association with arterial hypertension is possible because of the fact that with the latter condition, sclerosis of the small arterioles—arteriolosclerosis—is usu-

[1] Presented as the symposium on Hypertension before the Clinical Congress of the American College of Surgeons, San Francisco, October 28-November 1, 1935

ally present in the more advanced stages Bell (2) states that typical clinical cases of hypertension are frequently seen in which no arteriolosclerosis is found He cites this as a fact in support of the view that arteriolosclerosis is not the cause of hypertension

In this condition the most recently expressed view of Bell (3) is "It seems more satisfactory at present to use arteriosclerosis in a broad sense to include all non-inflammatory forms of arterial disease and to recognize, as Hueck does, that it is a collective term embracing a number of different processes which may or may not have a common etiology Special types may be distinguished on a basis of anatomical structure until distinct etiological factors are determined " Within the broad group of arteriosclerosis, he considers arteriolosclerosis a special anatomical type, "apparently due to increased intravascular pressure " We have no reliable information as to why certain vascular areas are affected and others are not

It is probable that there is no living pathologist whose work has been more widely accepted or whose views have been generally accorded greater respect than that of Aschoff In his introduction to the volume on arteriosclerosis by many writers, published in 1933, he has summarized his views and given his definition of the functional, degenerative and dystrophic diseases of the vascular system Extensive and necessarily incomplete quotations would wrench his statements from their context, but an attempt will be made to put in very succinct form some of the views he expresses In contradistinction to arteriosclerosis, an affection of the arteries properly so called, arteriolosclerosis is an affection of the precapillary arterioles, "usually manifesting itself by hyaline and lipoid imbibition on the part of the vascular walls which swell up to such a degree that the lumen may be completely occluded " It is fairly certain that its origin is in a functional stimulation of the vascular system which manifests itself by hypertension In the incipient pre-arteriolosclerotic state, the arterioles may still be quite free from actual disease The not infrequent bursts of hypertonia in early years are evidence of its independence of arteriolosclerosis Hypertonia leads to disease of the smallest arterioles, especially of certain organs (heart, kidneys, brain), especially if it becomes fixed in the course of advanced years "If it is at all justifiable to advance an opinion at this time, it would seem that the hypertonia is to be regarded as the cause of arteriolosclerosis of these vessels "

In a recent contribution to the discussion on elevated blood pressure, Volhard distinguishes "pale hypertension" from "red hypertension " He discusses the relative importance in each of the chemical or hormonal, and the nervous regulatory mechanisms In the first group, the patients are pale which he believes must be caused by contraction of all vessels, arising through a chemical, humoral mechanism only In this group belong nephritic patients with a tendency to develop angiospastic retinitis He says "It is difficult to imagine that a hypertensive condition in which the arteries of the brain and the retina are constricted can be brought about by a nervous mechanism " Pale hypertension develops also in certain forms of chronic hypertensive disease leading to deterioration of kidney function and malignant hypertension It is his conclusion that a two-fold relationship probably exists, the vasoconstricting substance or substances being the product of a diseased kidney and also a toxicant to the kidney, leading to renal insufficiency through lasting circulatory disturbances Of his red hypertension, the group today usually called genuine or essential, he says "It is easier to state what it is not, than what it is It is neither caused by general vasoconstriction, nor is it of chemical nor of purely nervous origin It is not, as the author earlier used to believe, of renal origin " He stresses the fact that this red hypertension is prominently a disease of old age, very seldom occurring before 30, rarely before 40, frequently between 40 and 50, and most commonly between 50 and 70 years of age He is inclined to believe that heredity, besides age, plays an important rôle, and he feels inclined to credit the existence of a hypertensive constitution, instead of the usual assumption of an abnormal excitability of the vascular system He leans more to the assumption of an inferiority of the vascular system mani-

fested perhaps through an early vasoneurosis but states "It is, however, possible that the wear and tear of a normal vascular system become accelerated through an inherited vasolability expressing itself by abnormally strong and frequent blood pressure fluctuations of nervous origin."

Volhard considers red hypertension a benign disease in so far as the kidneys are concerned, a benign nephrangiosclerosis, and he distinguishes a cardiac, cerebral, or pancreatic course of the condition. On the basis of this benign condition in certain cases the splanchnic and renal angiosclerosis may suddenly develop into a malignant and progressive renal disease, renal insufficiency and true uremia, the contracted kidney Volhard shows that the sudden turn in the course of the disease has never been fully understood but considers the development of a vicious circle in which the renal vessels become less and less capable of dilatation the free vasomotor play diminishes, and the renal blood supply becomes smaller and more dependent on the blood pressure which becomes more stable at a high level.

Recent advances have given information of a fundamental character as to the functions and interrelationships of the glands of internal secretion. Witness the clearly demonstrated functional relationship between the pituitary and ovaries. While it is clear that certain cases of arterial hypertension result from disorders of some member of that group known as the endocrine glands, a small percentage of the cases of suprarenal tumor being the clearest illustration it must be recognized that the common malady known as essential hypertension is not due to structural abnormality but that if the endocrine system is involved in the production of essential hypertension, the method of that production must be an essentially normal one involving the mechanisms of the autonomic nervous system. Reactions that are normal in character may be excessive in degree and may be elicited over excessive periods of time and by stimuli less than those required by the average individual. Individual differences in reaction to the same stimulus exhibited by members of the same animal species are among the most interesting phenomena in physiology and are well known by the experimental physiologist working with lower animals. Such great differences are seen every day in the reactions in man to a stimulus or to a drug and the clinician is ready to credit their occurrence in the field under discussion.

During the period when essential hypertension was regarded as a result of primary disease of the kidney with the retention of pressor substances, these substances were generally thought to be the end-product of protein metabolism At another time the excessive ingestion of protein food was considered. The appearance of hypertension in many gouty subjects drew attention to purine metabolism. Fat and lipoid metabolism have been the subject of much attention in two directions the first being the frequent relationship between essential hypertension and obesity and the second relating to cholesterol metabolism. Experience teaches that in the obese with hypertension, dietary restriction and weight reduction are often accompanied by a very satisfactory reduction in average blood pressure readings, but many of the obese without evidence of cardiac weakness have readings which are normal and below normal There have been many facts suggestive of a relationship to cholesterol, particularly because of its intimate relationship to arteriosclerosis. Even in this condition, however Wells looks upon the lipoids not as a primary factor but a secondary Carbohydrate metabolism has received attention largely because of the frequent occurrence of hypertension in elderly diabetics, and also because hyperglycemia is not uncommon in essential hypertension. The relation of sodium chloride in the organism has received attention, and other electrolytes of the blood have been and are being studied. Overeating in general, gluttony was long held to be the cause of hypertension However no constant relation between any of these factors and hypertension appears to exist, and it seems more than probable that the constitutional tendency to hypertension, whatever may be its cause, is the most important factor in the appearance of the hypertensive state. Some of these factors may be considered as remote or even

precipitating, but their inconstancy in essential hypertension makes a primary relationship impossible

In a recent paper the author discussed the part played by heredity and by hyperirritable vasomotor mechanisms in the causation of essential hypertension The opinion is expressed that heredity acting through excessive pressor responses on the part of the individual, is the dominant factor in producing the condition In the early stages, the blood pressure shows a marked excessive lability with upward excursions far greater than those shown by normal individuals It has been shown that differences between the lowest and the highest systolic pressure of 30 and 40, and often as great as 60 to 70 millimeters of mercury and more, may be readily obtained Changes in diastolic pressure in the same direction but of lesser degree occur with resultant and significant elevations of mean pressure In the normal individual examined under similar circumstances, the fluctuations are seldom greater than 20 millimeters systolic pressure and 8 to 10 millimeters diastolic pressure We occasionally see in the clinic, individuals whose basal or resting blood pressure is normal and does not exceed, let us say, 140 millimeters, who exhibit while under certain stresses, elevations of pressure much like those shown in the labile stages of hypertension The fluctuations may be obtained in a patient lying comfortably and passively in a semi-darkened room, the only variant being the subject of conversation by the examiner If matters causing concern, anxiety, worry, or irritation are introduced, sharp elevations of pressure may occur Leave the patient lying quietly alone, cautioned against any attention or response when the examiner returns, and, on returning, measure the blood pressure it will be found that a greatly lowered reading may be obtained These fluctuations are affective phenomena in response to emotional states They are brought about by mechanisms in the nervous system, normally in operation but abnormal in the degree of response In the individual with fixed or permanent hypertension, the basal level from which they arise is also abnormally elevated

The complex mechanisms in the nervous system involving end-organs, afferent and efferent pathways, centers and reflex arcs, are outside the scope of this paper Their discussion belongs in normal and pathological physiology, but no clinician, either medical or surgical in his outlook, can afford attacks on this problem without profound fundamental knowledge in the field

The lengths of time during which a patient may sustain essential hypertension in a benign, relatively harmless form are not yet known Individual variations both in the length of time and in the height of the pressure sustained are so great that no accurate relationship between the two can be found It is true in general that the higher pressures are less well borne There is a difference, difficult to explain, in the individual tolerance on the part of the cardiovascular system to the unusual stresses Some individuals whose recorded pressures are in the lower hypertensive ranges succumb relatively early, while a smaller proportion of those in the higher ranges respond to these stresses with surprising endurance The cause for these deviations from the expected can only be surmised Constitutional, probably inherited, differences in the resisting power and tissue reaction on the part of these different individuals would be an adequate explanation The actual cause is yet unknown I have recorded one patient, aged 85, on whom I have records of hypertensive readings beginning 25 years ago Two years ago at the end of 23 years of observation, the evidences of cardiovascular or renal damage in any form whatsoever were minimal I have no records on other patients covering a similar length of time but have a few records covering periods of 10 and 12 years

Why it is that a small proportion, approximately 10 to 15 per cent, of the patients with essential hypertension develop the so called malignant form is not known These patients might well be individuals with a cardiovascular renal system particularly susceptible to hypertensive stresses inherited or otherwise, but such factors have not yet been established

In 1933 Hines and Brown described a standardized test for measuring the variability

of blood pressure utilizing the effect of cold applied to the hand and wrist opposite the arm used for studying the blood pressure response. This test which is easily performed, makes it possible to study the reactibility of the pressor mechanism in large numbers of individuals. They conclude that at least 98 per cent of all subjects with hypertension of the essential form exhibit excessive reaction to local cold They state that normal subjects can be grouped as those with minimal and those with excessive responses of the systemic blood pressure to sensory and psychic stimulation. The character of the pressor response to local cold has been confirmed by others (5 7 12) In a further report of which they have shown me the manuscript, Hines and Brown (10) report studies in 571 normal and hypertensive subjects and amplify their original conclusions. They classify the subjects into (1) "normal reactors," (2) "normal hyper reactors" and (3) "essential hypertension." It is of special interest that of 8 hyper reactor normals they reported in 1932 3 had developed at this time clinical degrees of essential hypertension with elevation of blood pressure and demonstrable hypertensive changes in the retinal arterioles. They submit the conception that essential hypertension affects only subjects who are hyper reactors and that an abnormality of essential hypertension is an excessive response in the blood pressure to intrinsic and extrinsic stimulation.

The writer has been studying for many years the blood pressure response to emotional states in hypertensive patients and has attempted management of the early labile stages, with a view of shortening the periods of each day during which the blood pressure is elevated and of lengthening and multiplying the periods of lower pressure. This is based on the definite opinion that the too frequent recurrence of these excessive responses is the primary factor in producing higher and more fixed elevations of blood pressure along with cardiac hypertrophy and vascular changes Thus the proper emphasis in the management of essential hypertension lies in the control of the frequency and character of the emotional stimuli and of the affective pressor response This requires understanding of the patient s problems, much patience and ability in instruction, and leadership on the part of the physician. The purpose in management is to modify the environment and its effect on the pressor responses. We may not be able by rational methods to control the degree of response to a given stimulus, since this degree appears to be inherent in the mechanism of each individual. We can, however by control, shorten the periods of heightened pressure and lengthen the periods of lower, basal, or near basal pressure. The methods of approach to these problems will vary with every physician. No attempt at detailed explanation of any method of treatment can be attempted here I have learned however, to follow certain principles and having followed them, have seen responses to management and control which, though not brilliant, have been very satisfactory I will cite 2 cases in briefest possible form

CASE 1 J., male, was first seen in 1921 at the age of 57 years and a diagnosis of essential hypertension was made. In the first 5 years of observation, the highest pressures found were 210/118 and the lowest were 185/100. In 1923 gastro-intestinal symptoms developed, evidences of duodenal ulcer were found and medical management was undertaken, but bed rest was refused. Ambulatory treatment was inadequate and acute perforation required gastro-enterostomy on May 20, 1926. On June 18, 1931, cholecystectomy for gall stones was performed During the year preceding the last operation, the highest readings obtained were 215/105 and the lowest, 162/82 Although he showed marked lability of pressure and some response to relaxation, I felt that because of his gastro intestinal condition and of undue stresses in his business and his family satisfactory control was not secured. Following the operation and at my insistence, radical adjustment in his responsibilities was made. He gave up many tasks and responsibilities he had been carrying for others and for the community This was done willingly and with his full co-operation and understanding When these adjustments had been secured and for a period of nearly 4 years following, pressures on beginning an examination were usually in the order of 200 110 to 185/100 and after a few moments' rest, pressures near and about 145/85 were commonly secured. At the end of this 4 year period, increasing responsibilities in his business through death of a brother together with a resumption of certain favorite community responsibilities, were followed by return of pressure to nearly the readings given for the first year Since then the condition has seemed almost stationary except for the development of evidences of moderate left

ventricular hypertrophy He is an active and effective man of 71 years now, 14 years after the discovery of his hypertension, moderately controlled over the greater part of this time with a period of nearly 4 years of amelioration of the high pressure brought about, I believe, by management with his intelligent co-operation The program was broken up later by unavoidable causes

Conditions in the second case were very similar

CASE 2 W, first seen in 1923 at the age of 55 years, an alert, strenuous and effective bank executive exercising a great deal of supervision and spending long hours at his work A mild arthritis for which he had sought advice subsided under management The blood pressure reading secured on the initial examination was 165 systolic and 100 diastolic Similar readings were secured at long intervals, but were disregarded by him until 1927 when blood pressure records of 180/95 and 170/100 were secured during a strenuous reorganization and expansion program on the part of his institution A full exposition of his situation and needs was made to him Complete co operation was secured, and for 3½ years, readings at 3-month periods or oftener showed, as first records, for each visit such as 145/82 to 158/88, and after a few minutes' relaxation on the examining table, repeated records such as 128/79 and 132/78 were made At the end of the 3½ year period, an osteo-arthritis involving the spine, the hip girdle and the shoulders, elbows, and wrists began to be manifest again and with this, pressures near his 1927 figures developed and showed some unfavorable progress for the 4 years that have elapsed Osteo arthritis made a profound and unfavorable impression upon him because of previous history of the affection in his family

These are not isolated cases nor are they very common

In the majority of cases the foundation for management is laid during the first interview and just as soon as it can be determined that we are dealing with the essential type of hypertension, two purposes are kept in the foreground and maintained throughout The first is to demonstrate to the patient that some drop in pressure can be secured by rest and relaxation The patient is not allowed to see the manometer during the period of study of blood pressure but when the examination is finished, is informed of the readings with particular emphasis on the degree of lowering secured The second purpose in management is to acquaint the patient with the fact that essential hypertension is usually a benign disease and that, with proper co-operation and attention to his condition and his emotional responses the usual outlook is favorable Attention to these points is necessary because if not forestalled, the patient often develops from his relatives and friends a very distorted and pessimistic outlook One of the most curious gestures by the friends of any one in whom some malady has been discovered is to carry to him with all the horrendous detail possible innumerable stories of this or that one gone to his fathers by the same route The early anticipatory recital of the state of health and strength of one or more long-lived patients goes further in my experience toward establishing a favorable viewpoint than does a more theoretical discussion even though the latter is backed by real knowledge of the subject I attempt also to convince the patient that the problem and course of some other patient whose disorder has the same name or who may have one or more of the same symptoms are in no sense his problems and course The warning requires reiteration throughout the course of management I have said elsewhere and repeat here that I am sure that one of the most vicious effects of neighborhood medicine is to wreck very many well thought out and intelligently conceived medical programs which would otherwise be effective

It has been my experience that one of the most effective measures in the management of the early and labile stages of essential hypertension is to furnish the patient with knowledge of, and repeated experience in, the lowering of blood pressure to be secured by relaxation If he can be shown that when he is relaxed and serene, his blood pressure is lowered, but when he is on tension, hurried, and worried, his pressure is up, and can be shown this very early, he himself will have an understanding of the benefits of relaxation and through his own knowledge will be ready to cooperate For this reason it is my custom to tell a patient at the end of an examination what the entire series of blood pressure readings have been, with an explanation for the differences I give the exact readings I have at once secured his interest in a procedure novel to him, have secured his confidence, and have shown him something he does not know about blood pressure This sounds too simple

of blood pressure, utilizing the effect of cold applied to the hand and wrist opposite the arm used for studying the blood pressure response. This test, which is easily performed, makes it possible to study the reactibility of the pressor mechanism in large numbers of individuals. They conclude that at least 98 per cent of all subjects with hypertension of the essential form exhibit excessive reaction to local cold. They state that normal subjects can be grouped as those with minimal and those with excessive responses of the systemic blood pressure to sensory and psychic stimulation. The character of the pressor response to local cold has been confirmed by others (5 7 12) In a further report of which they have shown me the manuscript, Hines and Brown (10) report studies in 571 normal and hypertensive subjects and amplify their original conclusions. They classify the subjects into (1) normal reactors," (2) normal hyper-reactors" and (3) "essential hypertension. It is of special interest that of 8 hyper-reactor normals they reported in 1932 3 had developed at this time clinical degrees of essential hypertension with elevation of blood pressure and demonstrable hypertensive changes in the retinal arterioles. They submit the conception that essential hypertension affects only subjects who are hyper reactors and that an abnormality of essential hypertension is an excessive response in the blood pressure to intrinsic and extrinsic stimulation

The writer has been studying for many years the blood pressure response to emotional states in hypertensive patients and has attempted management of the early labile stages, with a view of shortening the periods of each day during which the blood pressure is elevated and of lengthening and multiplying the periods of lower pressure. This is based on the definite opinion that the too frequent recurrence of these excessive responses is the primary factor in producing higher and more fixed elevations of blood pressure along with cardiac hypertrophy and vascular changes. Thus the proper emphasis in the management of essential hypertension lies in the control of the frequency and character of the emotional stimuli and of the affective pressor response. This requires understanding of the patient s problems, much patience and ability in instruction, and leadership on the part of the physician. The purpose in management is to modify the environment and its effect on the pressor responses. We may not be able by rational methods to control the degree of response to a given stimulus, since this depends appears to be inherent in the mechanism of each individual. We can, however by control, shorten the periods of heightened pressure and lengthen the periods of lower basal, or near basal, pressure. The methods of approach to these problems will vary with every physician. No attempt at detailed explanation of any method of treatment can be attempted here I have learned, however to follow certain principles and having followed them, have seen responses to management and control which, though not brilliant have been very satisfactory I will cite 2 cases in briefest possible form

CASE 1 J male, was first seen in 1911 at the age of 57 years and a diagnosis of essential hypertension was made In the first 2 years of observation, the highest pressures found were 210/118 and the lowest were 185/100. In 1923 gastro intestinal symptoms developed, evidences of duodenal ulcer were found and medical management was undertaken, but bed rest was refused. Ambulatory treatment was inadequate and acute perforation required gastroenterostomy on May 20, 1926. On June 28, 1929 cholecystectomy for gall stones was performed. During the year preceding the last operation, the highest readings obtained were 215/103 and the lowest 164/82 Although he showed marked lability of pressure and some response to relaxation, I felt that because of his gastro-intestinal condition and of undue stresses in his business and his family satisfactory control was not secured. Following the operation and at my insistence, radical adjustment in his responsibilities was made. He gave up many tasks and responsibilities he had been carrying for others and for the community This was done willingly and with his full co-operation and understanding When these adjustments had been secured and for a period of nearly 4 years following, pressures on beginning an examination were mostly in the order of 200/110 to 185/100, and after a few moments' rest, pressures near and about 145/85 were commonly secured. At the end of this 4 year period, increasing responsibilities in his business through death of a brother together with a resumption of certain favorite community responsibilities, were followed by return of pressure to nearly the readings given for the first year Since then the condition has seemed almost stationary except for the development of evidences of moderate left

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15 WHITE, S M The status of the essential hypertension problem Michigan State M J, in press

to be true, but the effect is usually profound, and I am given as much opportunity for control as the mentality and circumstances of the patient will allow We are dealing with different capacities to receive impressions and to work out effective programs. If radical changes in the philosophy of life and in those segments of the environment responsible for undue stresses can be successfully engineered a pronounced shortening of the high pressure periods can be brought about. This may result, and in my experience has repeatedly resulted in a virtual disappearance of the major blood pressure elevations. I am referring here only to the early labile phases before organic changes have become demonstrable and before persistent fixed pressure elevations have *developed*.

I have attempted to place the emphasis in management of essential hypertension on the early labile phases and would include here those individuals whose basal pressure may not be that of the definitely hypertensive but who show pressor hyper-reactivity The discovery of these individuals in the early stages of the condition is a major problem in medicine. Life insurance examination, health examination and the adoption of blood pressure determination as a routine in all clinic and hospital admissions result in the discovery of a fair proportion of these cases Student health services in colleges and routine examinations in schools should take further note of hyper reactors and provide for follow-up since it is at this stage that environment and emotional control should be most effective

The prevalent practice of recording the lowest pressures secured rests on the false assumption that these are the characteristic pressures. It is my belief that the characteristic pressures are the highest ones to be secured under stimuli in general of an emotional character To learn the order or degree of stresses sustained these stimuli should simulate as nearly as possible those in the environment normal to the individual I have found the results of the local cold stimulation test of Hines and Brown, previously referred to parallel quite closely to the results of study of emotional pressor response. The ease of application and the definite reaction make it a satisfactory procedure for the routine testing of large numbers of subjects. It discovers certain hyper reactors *not otherwise* readily found When thus discovered, a study of emotional factors will usually reveal similar reactions The utmost importance attaches to the discovery of hyper reactors and early hypertensives in early life.

Discussion of the management of the later more severe, fixed and malignant types of hypertension and of the results of organ damage in essential hypertension is not desirable here. While it is true that in these phases the most favorable time for effective management has passed much can be accomplished by readjustment of the environment, readaptation to that remaining environment *that cannot be changed and by retraining and* reconditioning the individual. Specific regimens of rest of drugs, of diets, and of deprivations, such as of common salt, are not the answer to our quest for an effective therapy A high degree of individualization in management is necessary and, with it, gratifying results are often obtained. Until or unless we possess more adequate knowledge of the pressor mechanisms and factors conditioning them, we must be content with medical methods short of the ideal, but still measurably effective.

A surgical attack on the pathways of the pressor mechanism is mutilating to the nervous system and can be *justified only in certain* rare instances and with avoidance of disabling effects other than those on this mechanism It is to be hoped that papers in this symposium will make clear the indications for surgical procedure. We recall the great service rendered by surgery when it added to our knowledge of living gastric and duodenal pathology In the process, the indications for gastro-enterostomy were not clarified early and the operation was popularized and was performed in many quarters and by many men unnecessarily One is justified at this time in expressing the hope that procedures less severe, less crippling and non-operative in character may *be found before a corresponding* number of ineffectual operations are performed in the demonstration of the pathological physiology of essential hypertension.

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CEREBRAL INJURIES DUE TO EXTERNAL TRAUMA[1]

GEORGE W SWIFT M D F A C S Seattle, Washington

CEREBRAL lesions due to external violence challenge the ability of the surgeon to diagnose accurately the extent of injury to the skull meninges, blood vessels, water reservoirs and cerebral tissues to give immediate and continuous personal attention during the first few hours and careful direction for the following few days so that the accepted medical and surgical procedures are properly executed to prevent the unnecessary post traumatic sequelæ so common to these accidents, by the proper selection of immediate personnel with whom the patient will be associated during the period of unconsciousness and later readjustment to unusual conditions to assist in the establishment of hospital equipment service, and personnel so that emergency cases may have the advantage of the correct treatment during the first 3 hour period to train nurses and interns in their various duties so that they may do their part in the treatment of these cases to keep accurate records and publish from time to time the results of the successes and failures from this or that method of treatment in order to give others the benefit of this work and these observations to apply the laws of cerebral hydrodynamics and the pathology of altered normal physiology as it applies to this problem

This is the challenge to the surgeon of today How well it has been answered in the past 15 years is well known to all who are conversant with the literature, but of late there has crept into the reports and discussions of this problem, a note of pessimistic fatalism not in keeping with the traditions of surgery advice tending to trust the care and future of the injured person to the tender mercies of time, aided by the proverbial ice bag at the head and a prayer at the foot of the bed, and watchfully awaiting a sign or symptom demanding surgical relief seem to be heralding a return to the period of the early twenties rather than boldly accepting and mastering and teaching the lessons learned during the early thirties It is a challenge which we cannot put aside.

Each year approximately 125,000 injuries involving the head and spine occur in America Th number mounts year by year as the result of increased speed of transportation and mass production in industry America is on the move and we must do our part in meeting these accidental casualties of modern mania for speed in all of life s activities

During the period immediately following the war there was no accepted method of treatment for severe cerebral injuries, except in the cases of compound depressed fractures or intracranial hemorrhage when operative measures were universally employed decompression operations were advised whenever the pulse pressure and pulse rate crossed spinal drainage and the use of hypertonic solutions intravenously were not at that time universally employed Classification of injuries and reports were based upon the particular region of the skull and brain involved rather than upon the character and type of injury A sufficient number of cases reported had not as yet shown the relative importance of various methods of treatment or the other factors which are involved in the present conception of this problem. A report of our work covering the cases treated at the City Emergency Hospital in Seattle during the years 1919 to 1924 showed (Table I) 178 cases, with a mortality of 60.7 per cent The report classified the cases as to location of the fracture and part of the brain involved The operative incidence was 18 per cent and the operative mortality was 37 5 per cent. This is indeed a sad report compared to the present day statistics, and yet it was an accurate, though disheartening record

With the advent of the use of hypertonic solutions for the control of intracranial pressure with the better knowledge of the purpose of the reservoirs of fluid within the ventricles and cisterns of the brain and the method of preserving these water reserves and measuring the water content of the blood with better knowledge of the value of spinal drainage and decompression operative pro-

Presented before the Clinical Congress of the American College of Surgeons, San Francisco, October 28-November 1, 1935

cedures, with the increased value of blood and pulse pressure in the determination of the relative clinical condition of the patient, the mortality rate has been essentially lowered Of greater interest perhaps is the lowered morbidity rate and prevention of post-traumatic sequelæ as the importance of the use of these measures has been revealed during the past few years

In 1932 a second report covered the early period after the establishment of certain fundamental principles of practice which may be termed routine procedures in the management of cerebral injury cases Hospitals had been supplied with charts for the use of the internes and nurses, glucose solutions of various strengths were kept ready for instant use, hasty and useless X-ray examinations during the 12 hour period were eliminated, shock symptoms were recognized, and the early treatment for this distressing complication devised These measures lowered the mortality, morbidity, and operative incidence In the new King County Hospital (Harborview) had been organized a department of neurosurgery, equipped to offer the best immediate treatment for these cases Our report for the first 45 cases treated (Table II) at the new hospital revealed a gross mortality of 35 5 per cent while 145 cases treated during 1930–1931 in 6 private hospitals in Seattle showed a gross mortality of 24 8 per cent The difference between the two is accounted for by the fact that after Harborview was opened, most of the severe cerebrocranial injuries were sent there first and transferred to private hospitals after the immediate danger had passed

In this study no effort was made to segregate the cases as to the location of the injury, as in our previous report, but we attempted to classify the cases as to "time elapse" and mortality figures This was in line with other reports in large centers

Treatment procedures were observed and recorded (Table III) in a series of 64 cases treated in private hospitals, as follows

1 Rest only—ice bag and sedatives with a mortality of 21 per cent These were, of course, the rather mild cases

2 Rest and use of dehydration measures Mortality dropped to 14 per cent

TABLE I—SUMMARY OF 178 HEAD INJURY CASES TREATED AT THE SEATTLE CITY HOSPITAL, 1919–1924

Region of fracture	Cases	Died	Mortality per cent
Frontal	46	29	63 2
Middle	42	22	52 8
Posterior	14	9	64 3
Basilar	76	48	63 2
Total	178	108	60 7
Operated upon	32	12	37 5

3 Operation before the use of dehydration measures with 50 per cent mortality

4 Operation after the use of dehydration measures, 46 per cent mortality

The gross mortality in the 64 cases was 26 5 per cent

The gross mortality of 35 5 per cent in severe emergency cases at Harborview was a marked improvement over the 60 7 per cent at the old City Hospital (Table IV) Segregation into time periods rather than location of injury gave us a different angle from which to study our results

In 1933 we reported on the first 175 cases treated at Harborview Hospital These patients were admitted between March 1, 1931, and December 1, 1932, or in a period of 21 months, an increase of 300 per cent in the incidence of head injuries in a 10 year period The gross mortality for these 175 cases was 22 4 per cent For the first time, another careful check was made regarding ages, and we began to recognize a new factor and one which we will stress later (Table V) In Table V we have recorded the age incidence in 163 cases

AGE AS A FACTOR IN INJURY AND MORTALITY

That age should be a factor in both the incidence and mortality of head injuries would, at first thought, not appear to be important yet careful study reveals it to be a fact The many "safety first" and "save the children" campaigns and traffic regulations have materially decreased the incidence of injury to children Children also are seen to withstand severe head injuries better than adults, and the morbidity is never so high as in older patients The gross mortality has remained about the same throughout Rarely does one

TABLE II—SUMMARY OF 190 SEVERE CASES OF CEREBROCRANIAL INJURIES JANUARY 1930—NOVEMBER, 1931

Hospitals	Cases	Physicians	Operations		Mortality							Improved cases			
					Total		Within 24 hours	Final mortality	Operations		Non-operative	Operations	Hospitalization Ave No days per case		
	Total No	Total No	Total No	Per cent	No	Per cent	No	Per cent	No.	Per cent	No	No	Entire series	Non-operative	Operative
A	18	20		5		5		14.3			4		4 days	days	17.3 days
B	17		6	42	4	8		3	3 within 24 hrs	50		3	3	3	33
C	44	35	3	34		27.3	8		5 3 within 24 hours	33.3	7	10	20.6	7.3	27.3
D	15		6	24	7	68	3	38	within 24 hours	33.3	3		7.5	10	7.3
E	24	16		66.6	8	3.3	3	33.8	4 within 24 hours	80	4		8.5	7.7	10
F	9	6		44		1							6	6.3	3.3
Total	3	85	38	26	36	14.8	18	14	5 within 24 hours	38.8	7	14	5		10
Harborview	5			4	26	33.3			within 24 hours	50	3		6	3.3	10

TABLE III—SUMMARY OF TREATMENT AND RESULTS OBTAINED FROM 64 CASES IN PRIVATE HOSPITALS, JANUARY 1930—NOVEMBER, 1931

Treatment	Cases	Mortality					
				Deaths within hours			Deaths after hours
	Total No	Total No	Per cent	No	Cause	No	Cause
Rest only ice bag tentative	33	7		3	Shock		Shock (24 hours) Hemorrhage or edema
Rest with either glucose or spinal drainage, or both	14				Hemorrhage and shock Shock		
Operation only			50		Hemorrhage and shock		Hemorrhage or edema
Operation after glucose or spinal drainage, or both	3	6	46		Hemorrhage and shock		Hemorrhage or edema Abscess of lung Meningitis
Summary	64	7	26.3		Shock Hemorrhage and shock	4	Shock (2 hours) Abscess of lung Meningitis Hemorrhage or edema

have to resort either to surgery or to spinal drainage. In the age period above 60 years, one expects a high mortality because of complications of a general nature, senile changes elsewhere in the body arteriosclerosis, nephritis, diabetes, and other general diseases

The period of greatest incidence of injury was between the ages of 16 to 45 years. Almost half of the injuries occur in this period and here we find the greatest morbidity and highest relative mortality This study prompted us to keep a more constant record of the cases of an age period between 30 and 60 years. We began to recognize certain basic facts and to realize that a problem presented itself quite different from the cases of injury in patients under 16 years of age and over 60 years. Factors in middle age which play an

TABLE IV —A COMPARISON OF THE FIRST AND SECOND REPORTS

	Cases	Mortality	Per cent
Seattle City Hospital 1918–1924	178	108	60 7
King County Hospital March–December, 1931	45	16	35 5

important rôle both as to the cause, and also as to the effect, of injury may include

1 The activity of persons of this age in hazardous occupations

2 The incipient stage of deterioration of the body mechanism

3 The beginning of the slowing up process in mental reactions

4 The effects of alcohol, hard labor, diseases and worry, which begin to show and to retard quick physical response to unusual demands

5 The failure of repair processes or the retardation of response which add to the morbidity

6 The disturbed water balance

Of these factors, we believe that disturbed water balance is the most important

CEREBRAL HYDRODYNAMICS

In 1928 I advocated the theory that the free water found in the ventricles and cisterns of the cranial cavity within and around the brain should be considered as reservoirs for the storage of water which is subject to instant demand on the part of the blood for use in the maintenance of blood volume I also advocated that nature had contrived this mechanism as an ingenuous device situated in the most convenient place of the body for instant use, had protected it by a bony enclosure, and that it was subject to the natural physical laws of hydrodynamics

As early as 1824, Kellie called attention to the importance of cerebrospinal fluid in maintaining blood volume Burrows later added his belief that it had an important rôle beyond protection Space does not permit a discussion of the details of our present conception, but the important factors bearing upon this problem may be mentioned and its relation to the reaction of patient to cerebral injury may be discussed

TABLE V —KING COUNTY HOSPITAL (HARBORVIEW) MARCH 1, 1931–DECEMBER 1, 1932 (21 MONTHS)

Ages*	Cases		Mortality		Mortality of age group of 175 cases	
	No	%	No	%	No	%
1–16	37	22	5	13	5	28
16–45	70	42	13	35	13	7 4
45+	56	34	23	41	23	13 1
Total	163		41		41	

*12 cases unrecorded

The points which support at least the theory of a water reservoir are

1 Location of water reservoirs within the bony enclosure of the craniovertebral cavity

2 Distribution of water reservoirs both outside and within the cerebral hemispheres

3 The presence of the enormously enlarged surface area of the choroidal plexuses, far more than the excretion of water alone would justify

4 The intricate mechanical arrangement of the Pacchionian and arachnoid villi along the dural and spinal venous system for the rapid reabsorption of water into the venous channels

5 The absence of water over vital surfaces and portions of the brain, such as the occipital and frontal lobes

6 Physiologically one might mention the proved ebb and flow of cerebrospinal fluid volume in sleep and wakefulness, the decrease in sudden changes in blood volume as in hemorrhage with undoubted signs of cerebral anoxemia, hyperactivity during the menstrual period and sluggishness or stupor in hydrated states following heavy meals or drinking

7 The demand for a variable to be present to act in any emergency, for the increase or decrease of blood volume is found ideally situated within the closed bony encasement of the craniospinal cavity subject to the laws of physics stated in the Monro-Kellie doctrine and later further elaborated and proved by Weed

These are the points which must be considered in any study of the location and protection, purpose, and function of the cerebrospinal fluid

TABLE II—SUMMARY OF 190 SEVERE CASES OF CEREBROCRANIAL INJURIES JANUARY 1930—NOVEMBER, 1931

Hospitals	Cases	Physicians	Operations		Mortality							Improved cases			
					Total		Within 24 hours	Final mortality	Operative		Non-operative	Operative	Hospitalization Ave. No. days per case		
	Total No.	Total No.	Total No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	No.	Entire series	Non-operative series	Operative series
A	16	10		1	4	1		3			4		11 days	11 days	11 days
B	17		6	12	4	8		5	3 within 24 hrs	50		3	14.3	11.5	13
C	44	37	5	34		17.3	8		5 within 24 hours	11.3	7	10	10.4	7.5	17
D	5		6	86	1	20	1	16	within 24 hours	33.3	5	4	7.5	10	7.3
E	14	18	5	10.8	8	33.3	3	3.8	4 within 24 hours	80	4		8.5	7.7	10
F	9	8	4	44.4								4	5	6.5	5
Total	45	87	28	16	36	14.8	12	14	14 5 within 24 hours	36.8	11	14	14.5	9	10.8
Harborview	45	4		4	16	33.5			within 24 hours	50	3		6	5.5	10

TABLE III—SUMMARY OF TREATMENT AND RESULTS OBTAINED FROM 64 CASES IN PRIVATE HOSPITALS, JANUARY 1930—NOVEMBER, 1931

Treatment	Cases	Mortality						
				Deaths within hours		Deaths after hours	
	Total No.	Total No.	Per cent	No.	Cause	No.	Cause
Rest only [illegible]	33	7	21	3	Shock	3	Shock (24 hours) Hemorrhage or edema
Rest with either glucose or spinal drainage, or both	4		24		Hemorrhage and shock Shock		
Operation only			50		Hemorrhage and shock		Hemorrhage or edema
Operation after glucose or spinal drainage, or both	3	6	46		Hemorrhage and shock		Hemorrhage or edema Abscess of lung Meningitis
Summary	64		18.5	4 4	Shock Hemorrhage and shock	6	Shock (24 hours) Abscess of lung Meningitis Hemorrhage or edema

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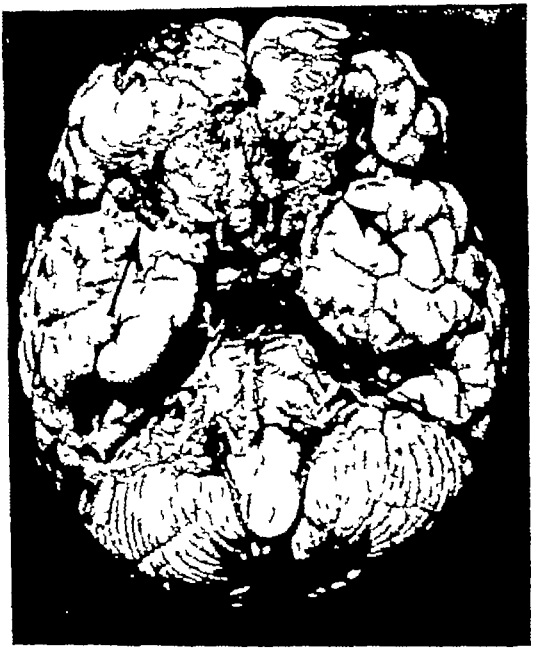

Fig 2 Direct trauma, anterior tip of the right frontal lobe. Indirect trauma to the inferior surface of both frontal lobes

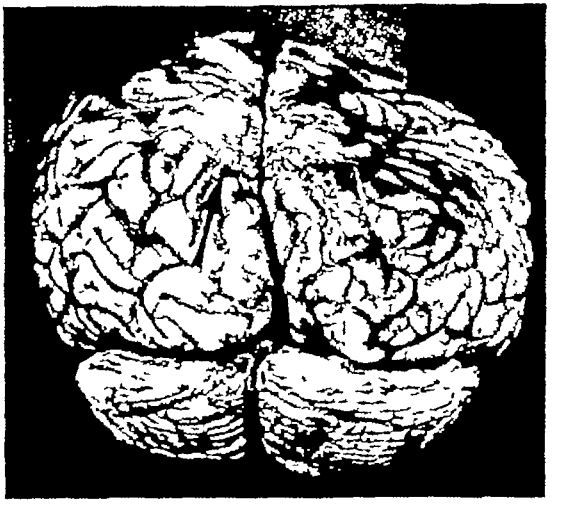

Fig 3 Contrecoup trauma to the superior occipital lobes Marked convolutional atrophy (chronic alcoholism)

this group of injuries—the convolutional atrophy (Figs 4 A and B)? Figure 4 A shows the lateral surface of the brain in the case just presented—a chronic alcoholic, Figure 4 B the same view of the brain of an adult epileptic An arteriosclerotic or syphilitic brain would present a similar picture Grossly the four pathological conditions present identical physical problems—they all have hydrated or "wet" brains—marked increase in the amount of subarachnoid fluid with consequent convolutional atrophy of the cerebral hemispheres They therefore present a major problem in cerebral injuries Since the hydrated or wet brain is more often present in persons after 40 years of age, it undoubtedly has a definite influence both on the incidence and subsequent mortality and morbidity of injuries occurring in this period

With these facts in mind, we have made a final study of the cases treated at the King County Hospital (Harborview) during a period of 6 months October 1934, to April 1935

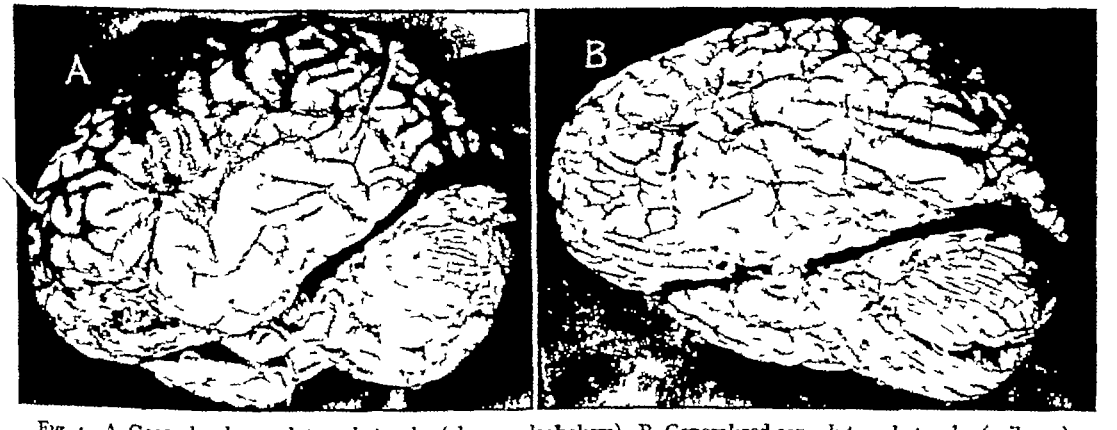

Fig 4 A, Generalized convolutional atrophy (chronic alcoholism) B, Generalized convolutional atrophy (epilepsy)

TABLE VI.—INCIDENCE AND MORTALITY IN 214 CASES IN 5 YEAR PERIODS

Note the low mortality below 5 and after 60 but the high incidence and mortality between 5 and 60 The highest incidence between 40 and 60 years King County Hospital (Harborview) October 1934–April, 1935.

Classified as to Ages

Under	5	10	15	20	25	30	35	40	45	50	55	60	65	70	75	80
No of cases	32	10	11	17	30	30	30	37	37	30	14	6				3
Dead	3	0	0		0	7	4	3	4		3			0		
Mortality—per cent	9 7	30		7 4	23	34	71	7	10	13	21	3	43			66

	0 to 5	5 to 40	40 to 60	60 to 80
No of cases	32	33	78	71
Dead	3	10	19	9
Mortality—per cent	9 7	30 3	24 4	6

Final mortality 214 cases—Deaths 41—19 per cent mortality

We have based our treatment of these cases upon the theory that

1 The damage is largely done by direct hydraulic pressure and in direct proportion to the character of injury

2 A disturbance to the normal cerebrohydrodynamics must be rectified at the earliest moment.

3. A maintained cerebrospinal fluid balance is essentially a determining factor both as to mortality and morbidity

4. Cerebral hemorrhage, when fatal occurs within the first 3 hours and in less severe cases may be controlled by proper spinal drainage.

5 The presence of a hydrated brain previous to the injury necessitates the most careful and constant observation

6. The controlling factors are blood pressure, pulse pressure and sustained nourishment of the patient during these hours of repair

7 Spinal drainage, hypertonic solutions, and whole blood transfusions are the most valuable procedures. They must be ordered only after careful evaluation of the demand for each one and under the constant supervision of trained nurses internes, and surgeons. Our results are shown in Table VI.

TABLE VII.—CHART SHOWING THE INCREASE IN THE INCIDENCE AND THE DECREASE IN MORTALITY OF HEAD INJURY CASES IN SEATTLE OVER A PERIOD OF 16 YEARS

Period	Cases	Mortality per cent
1929–1934 (five months)	178	60 7
March, 1931–December, 1931 (11 months)	71	23 3
October, 1934–March, 1935 (6 months)	114	19

From Table VI we may observe that the mortality in persons between the ages of 1 to 16 years is about the same as in our second report In persons over 60 and especially over 70, the mortality depends largely upon the general health rather than the specific injury If we are to lower the gross mortality it therefore follows that we must improve our treatment in the group of persons between the ages of 40 to 60 years. In this group we believe that the maintenance of water balance is a most important factor A summary of our study is shown in Table VII

CONCLUSION

In conclusion, may I again say cerebral lesions due to external violence challenge the surgeons of America to give immediate personal attention, to exert the utmost skill in diagnosis, to select proper personnel to assist the hospital in its share of work, to train internes and nurses, to apply the laws of cerebrohydrodynamics, to prevent unnecessary sequelæ to keep accurate records, and to publish the results. This is the challenge to the surgeons of America.

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THE DIAGNOSIS AND TREATMENT OF STONES IN THE COMMON BILE DUCT[1]

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DURING the last 20 years a radical change has taken place in the surgical treatment of biliary tract disease Cholecystostomy with removal of stones within the gall bladder was the only operative procedure that the pioneers in modern surgery dared to undertake when dealing with this structure Cholecystostomy gave relief to a considerable number of patients, but it soon became evident that too many of these patients had recurrent or continued symptoms, or were left with a persistent mucous or biliary fistula With the improvement in surgical technique and with added knowledge concerning the character of the disease, the operation of cholecystectomy gradually supplanted simple drainage in the majority of instances Cholecystectomy gave a higher percentage of cures and was on the whole a comparatively satisfactory procedure Exploration of the biliary ducts for a long period of time was resorted to only in the presence of prolonged jaundice, or when a large stone could be palpated within the duct, or, secondarily, when symptoms persisted after cholecystectomy Numerous surgeons were content to leave the ducts unexplored even in the presence of mild or moderate jaundice, in the hope that this feature of the process was due to a secondary inflammation about the outlet of the duct rather than to the presence of a stone within it

Gradually, we have come to realize that there are numerous factors other than jaundice that must be taken into consideration regarding the ducts when biliary calculi are dealt with When these factors are analyzed, it becomes evident that, in a large number of these patients, we may well overlook the more important pathological condition present by failing to explore the ducts Reports by various authors from clinical experience and postmortem examinations place the percentage of stones within the common and hepatic ducts from 12 to 20 in all patients with gall-bladder stones This percentage would indicate that, if we explore no ducts, we will fail to relieve a large number of patients As a matter of fact, the signs of a probable pathological process within the ducts are frequently present even though careful exploration fails to reveal stones Such stones may be high in the hepatic ducts or may be moved inadvertently to that position in which it is difficult to locate them and bring them down into position where removal is practicable If the duct is not particularly abnormal pathologically, small stones may pass through the papilla of Vater after cholecystectomy, since it is known that the sphincteric action of the outlet is at least temporarily lost after the gall bladder has been removed This probably accounts for the experience many of us have had, namely a typical attack of biliary colic occurs after cholecystectomy and the patient has ultimate spontaneous relief More often, however, these patients continue to have attacks of colic, and a secondary operation on the duct becomes necessary The irritation brought about within the outlet of the duct by inflammation and the trauma caused by the stones passing through the papilla may result in a constriction of this rather narrow orifice, which in itself will impede the flow of bile The result will be damage to the liver and a state of health incompatible with the ordinary activities of life

INDICATIONS FOR EXPLORATION OF THE BILIARY DUCTS

Roughly the symptoms and signs which cause one to suspect a pathological condition within the common or hepatic ducts may be divided into two mains groups (1) the pre-operative and (2) the operative Among the pre-operative signs and symptoms are (1) jaundice, active at time of examination or a part of the past picture, (2) continuation or recurrence of symptoms after biliary tract surgery, (3) chills and fever following epigastric pain, (4) frequent attacks of biliary colic,

[1]Presented before the Clinical Congress of the American College of Surgeons San Francisco October 28–November 1, 1935

Fig 1 Diagrammatic illustration of the exposure of the supraduodenal portion of the common duct with careful preservation of a border of the serous coat of the gall bladder and the areolar tissue overlying the ducts The incision in the duct is held open with fine silk gut sutures The lateral attachments of the duodenum may be freed as much as necessary for exposure Inset A shows the diagnostic separation of the duct with a small hypodermic needle

(5) severe nausea associated with attacks of typical pain (6) gall stones found in the stools before operation Among the operative signs and symptoms are (1) small stones or sand within the gall bladder (2) palpable stones within the ducts (3) contracted gall bladder (4) dilated cystic duct (5) dilated common duct (6) thickening in the head of the pancreas (7) gall bladder without stones (8) cholangitis

Immediately we see that many of these factors so obviously indicate the necessity of exploration of the ducts that the average surgeon would not fail to realize that any operative procedure without this step would be unsuccessful Also it is apparent that several of these signs and symptoms may occur together in the same patient It is only that we may not overlook some of the *less common* less well known or even less likely factors that they all must be considered.

Jaundice may occur coincidentally with gall bladder stones, or after the gall bladder has been removed. Even when pain has been present at the onset jaundice may be present and *still no stone may be found obstructing* the duct outlet. In some cases the obstruction may be found to be due to stone and yet biliary colic is not present. The possibility of the presence of a malignant obstruction should be considered and the region investigated before the gall bladder is removed as cholecystgastrostomy is a much easier and safer procedure than choledocho-enterostomy *However in the vast majority of jaundiced* patients with gall-bladder stones, we will find that the obstruction in the duct is due to the presence of a stone.

The continuation or recurrence of symptoms after biliary tract surgery is an embarrassing situation that few of us have escaped *It is true that even when a diseased gall* bladder has been removed and the ducts are found normal or when stones have been removed at the original operation a few patients continue to be unrelieved. The burden of proof however is on the surgeon to find the source of the symptoms in overlooked *disease of the duct One must not be content* with negative exploration as far as stones are concerned as in a considerable number of these patients who have had many operations in this region we find that the true situation is a constriction of the outlet of the duct Rarely symptoms may be due to postopera*tive adhesions, a most difficult condition to* evaluate and most unsatisfactory from the standpoint of treatment

Biliary colic with very frequent attacks is one of the most often overlooked indications for exploring the common duct The analysis of a large number of case records shows that *this symptom is often due to the passage of* small stones through the ducts, frequently due to disease of the duct alone and occasionally due to a single ball valve stone within the duct even though no stone be present in the gall bladder This warning may be of especial value in the patient with frequent attacks less than 1 week apart

Vomiting as a prominent symptom associated with biliary colic is an important indication of disease of the common duct This has been demonstrated by Zollinger who found that a collapsible bag inserted into the common duct under light anesthesia would when the patient awakened produce severe colic and nausea as soon as the bag was distended Although this experiment was made on a comparatively small number of patients the

Fig 2 A, Diagrammatic illustration demonstrating the method of palpation and exploration of the duct from the left side of the patient Obvious stones removed with fenestrated forceps B, The papilla is probed and dilated under palpation and partial vision Care must be taken not to damage the incision in the duct by an incorrect instrument and too much force C, The ducts are irrigated with normal salt solution in both directions Importance of suction tip is emphasized D E, and F A No 10 soft rubber catheter is transfixed with a small atraumatic needle carrying No 0 chromic catgut. These sutures fix the catheter within the duct, then are utilized to close loosely the opening in the duct and the areolar tissue over it The border of the preserved serous coat of the gall bladder is then closed, a minimum of unperitonealized area being left

symptoms coincide with the early history of many patients in whom common duct stones have been found at operation Zollinger further demonstrated that distention of the gall bladder would give epigastric pain but in none of his experiments did it produce nausea Nausea may develop in the later stages of gall-bladder inflammation without duct stone as the ducts become secondarily involved Also, this symptom may develop when the pancreas or duodenum become irritated, probably through the same nerve mechanism However, the patient with early nausea associated with common duct obstruction often comes to the hospital for treatment after this symptom has subsided, and for the same reason nausea may not appear as an important factor in the data obtained

Although the importance of the history and physical findings cannot be overemphasized we are so often left with no real clew indicating disease of the duct that in nearly every instance we must consider the possibility of common duct involvement at operation The only exceptions to this rule are represented by the extremely ill patient who submits to the life saving simple cholecystostomy and by those whose condition on the operating table

Fig 3 Diagrammatic drawing showing the method of holding the peritoneum, fascia, and skin upward and toward the left side while the stab wound is made in the right flank

precludes further prolongation of the operation after the gall bladder has been removed The common duct should be partially exposed in the supraduodenal portion by dividing the areolar tissue over it (Fig 1) Its size and inflammatory state must be determined. In many instances the duodenum will interfere with proper inspection and palpation of the duct region but it can be freed sufficiently without harm whether the attachments laterally are normal or pathological. The foramen of Winslow should be exposed sufficiently so that palpation of the ducts can be made in a logical manner In the average patient, the depth of this region makes palpation and inspection as well as operative procedures on the ducts, much easier for the surgeon if he stands on the left side of the table (Fig 2) Previously we described in detail the technique of operation on the common bile duct, and later we found that several resourceful surgeons had used this method of palpation of the duct region as a matter of course. Many others have told us since of their satisfaction in having adopted it. Stones within the duct that would elude the palpating fingers in the ordinary examination are easily detected if this method is used

Small stones and sand represent the most common finding in the gall bladder that makes common duct exploration logical That these small particles have found their way through the cystic duct is almost certain To be sure, they may have passed on through the papilla of Vater into the duodenum. At operation we often find, however that many of these particles are still within the ducts It is too much to hope or expect that they will always be discharged spontaneously With careful technique, the duct can be cleared of this débris with perfect safety If the papilla is dilated there is opportunity for a free flow of bile into the intestine, carrying with it unreachable stones and nuclei for future calculi of sufficient importance to eliminate the necessity of a secondary operation

When we encounter a *contracted gall bladder* we usually have a patient with a long history of difficulty in this region Doubtless when this condition is found incidentally it *represents nature's method of cure.* Many such patients with long remissions may finish out their lives without sufficient trouble to warrant surgical interference. Often, however difficulty develops within the dilated common duct, which represents the location of the active lesion, rather than in the gall bladder *itself. At times, it is wise to ignore* the original process as represented by the contracted gall bladder and to correct only the pathological process in common duct. Usually there are stones within the duct. Occasionally however the true condition is a constriction of the duct outlet, proximal to which is found inspissated bile, thickened duct walls, and liver damage. It is important not only to free the ducts of stones and débris but to provide for a normal flow of bile. If the decompression of the liver can be accomplished in such a manner as to allow drainage to take place into its normal habitat rather than to the outside, we will hasten the recovery of the patient and avoid prolonged external drainage which increases hospital stay and invalidism.

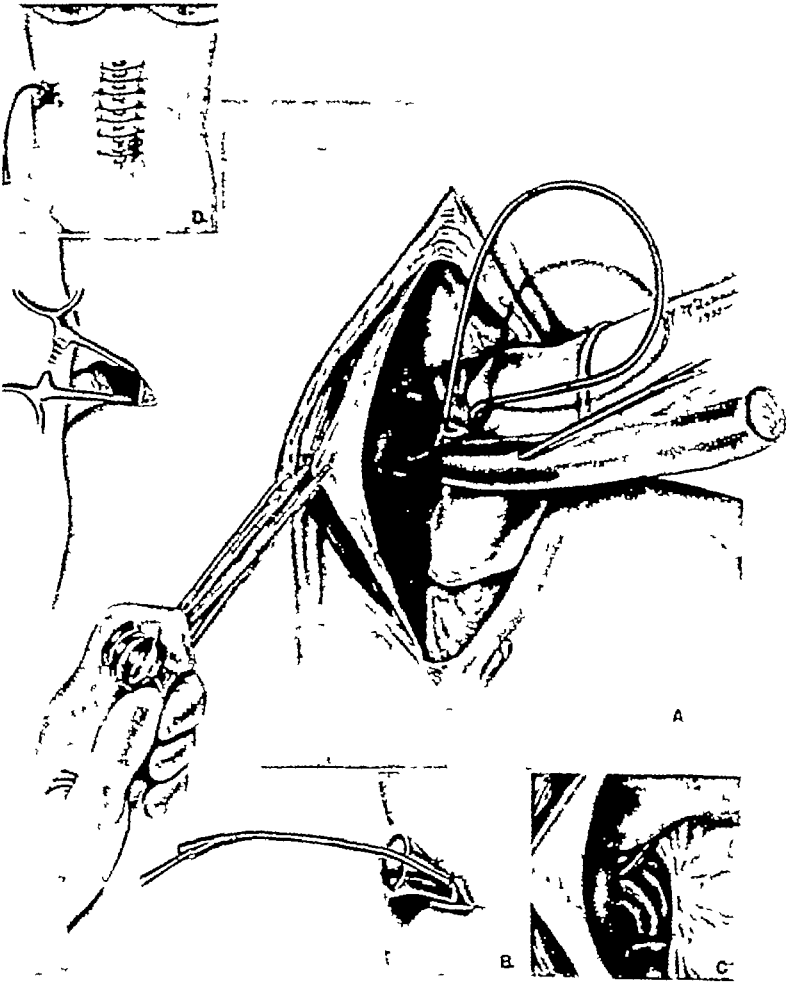

Fig 4 Schematic drawing illustrating the method of bringing the catheter and cigarette wick through the stab wound under direct vision, the duodenum and hepatic flexure being protected by omentum The catheter lies along the underneath surface of the right lobe of the liver and the cigarette wick is carefully placed in the subhepatic space of Morrison

Dilated ducts found at operation indicate as a rule disease within them If the cystic duct is large and patent in the presence of gall stones, we must assume that some and rarely all of these stones have passed into the common duct This often occurs in the absence of jaundice Although we frequently fail to find stones within the common or hepatic ducts, we do find them in a high percentage of such cases The average diameter of the normal common duct is approximately 5 millimeters When we find that this duct is larger than normal, we must assume that the abnormality may be due to disease within it That the common duct increases in size after cholecystectomy is well known This abnormal state may be reproduced through interference with the physiological mechanism by inflammation, by pressure from stone, etc in patients without previous operation The dilatation in many instances, however, is apt to be due to mechanical obstruction of the duct outlet Doubtless these various factors are often combined to bring about the increase

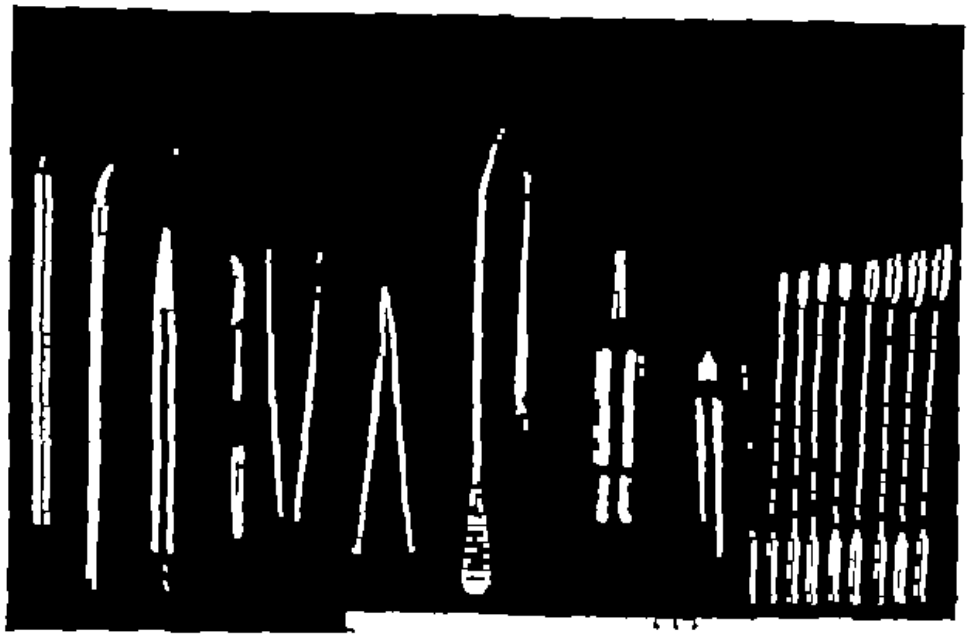

Fig 5 Photograph of instruments found useful in common duct surgery A small size suction tip has been fitted with hollow ground trocar point, useful in aspirating tense gall bladder The long curved scissors and fine tooth forceps are helpful in dissection The small curved knife is the safest instrument to use in opening the duct To the right are shown American made dilators after the Baker model The bulbs run from 3 millimeters to 11 millimeters in diameter

in the duct capacity Since it is impossible to know whether stones or a constricted outlet *are present we must explore these dilated* common ducts routinely

We so frequently find a definite *thickening in the head of the pancreas* associated with gall-bladder calculi that we cannot help but feel the significance of relationship between those two systems. The frequency with which gall stones are noted in the presence of acute hemorrhagic pancreatitis makes it difficult to dissociate the biliary system as an important factor in pancreatic disease. For this reason we have included in our gall-bladder statistics all cases of acute pancreatitis found at operation when the operative procedure included drainage of the biliary system. When the pancreas is felt to be thickened we look for fat necrosis, particularly in the underneath portion of the gastrocolic omentum. In the majority of cases, we find none. Rarely do acute manifestations of pancreatitis develop after the biliary tract has been explored Often however in the presence of pancreatic enlargement we find a dilatation or a thickening of the duct wall and occasionally a true inflammation within the ducts Stones or débris in the ampulla of Vater or a constriction of the outlet are so frequently associated *with this pancreatic thickening that we feel* justified in recommending exploration of the ducts in all such cases.

By the term *gall bladder without stones* we refer to the type of patient whose symptoms indicate biliary tract disease and who exhibits at operation little abnormality in the gall bladder itself Many of these patients with a positive Graham test will fail to show at operation, a gross pathological condition particularly stones. We have long been unhappy concerning the necessity of a microscopic diagnosis in cholecystitis. Even when gross cholesterolosis is found the removal of such a gall bladder in many instances, has *failed to relieve the patient of symptoms for* which the operation was undertaken Recently Graham and Mackay have shown that the highest percentage of unrelieved patients in gall-bladder surgery were those with minimal disease. *Although we can avoid surgery* in many of these cases by a more careful regulation of diet and by an evaluation of the functional elements concerned in neurotic individuals, we will of necessity operate upon some

such patients When a comparatively normal, stone free gall bladder is found under these circumstances, there may be a single ball valve stone within the common duct, or even rarely, several stones, without any apparent increase in the size of the duct or any actual thickening in the duct wall itself

Cholangitis varies so much in the condition found at operation, that often we are unable to remedy the situation by one procedure The ducts that are constricted, thickened, and full of débris are particularly difficult to explore and failure results Later the ducts may become dilated so that proper dilatation of the outlet and proper drainage permit a good recovery If the ducts are sufficiently large to permit exploration and drainage with dilatation of the papilla at the primary operation, the results are apt to be satisfactory It is believed that the earlier the operation in suspected cholangitis, the greater the possibility of a successful primary procedure

TECHNIQUE OF OPERATION

With the increasing consciousness of common duct stones associated with gall-bladder disease, it becomes imperative to develop a safe and satisfactory technique of duct exploration To avoid overlooking stones, the surgeon must necessarily open many more ducts than are found actually to contain stones, hence the surgeon must work out a plan by which he can explore the ducts and yet not damage them or increase the mortality rate An easy, simple, and safe procedure has been described in detail (2) It consists in exposing the duct in its supraduodenal portion, palpating it carefully from the left side of the patient, removing stones with the fenestrated forceps, probing the hepatic ducts and the papilla of Vater, then gradually dilating the papilla after the method of Bakes to a diameter just below that of the duct itself, or sufficiently to allow stones of the size present to pass through, if they have been overlooked or have become lodged within the hepatic ducts The ducts are then irrigated with normal salt solution and a No 10 F catheter is sutured in the incision in the duct and is led to the outside with a cigarette wick

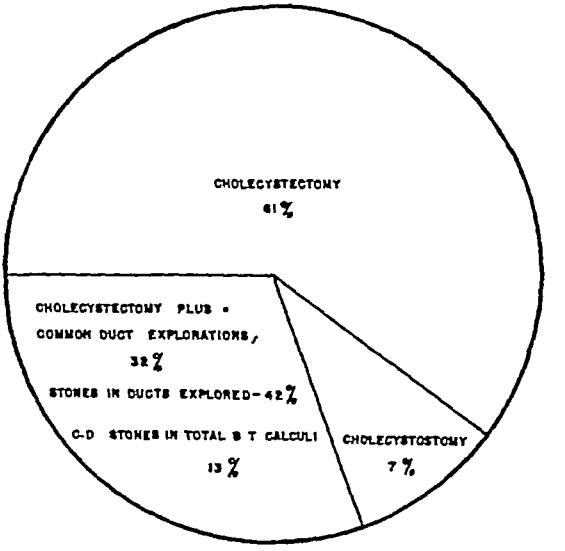

Fig 6 Biliary tract operations, Massachusetts General Hospital, October 1, 1930–October 1, 1935

The wick is placed in the subhepatic space of Morrison where all drainage from this region collects The wick and catheter are brought out through a stab wound below the twelfth rib This allows complete closure of the abdominal wound and when done under vision and with care is a rational procedure In a large series of patients so treated, we have had no complications from this procedure or cause to regret this type of drainage It shortens the hospital stay and decreases the number of infected wounds and incisional hernias

Routine dilatation of the papilla of Vater when the common duct is explored was first brought to our attention by Cheever He used for this purpose silk woven catheters, the sizes varying from a No 10 to No 20 F He found that the normal papilla would admit the No 10 size and that gradual dilatation could be carried out in almost all instances up to a No 20, without apparent damage to the tissue This commendable method allows irrigation through the dilating instrument—a step the value of which is enhanced by the flexibility and shape of the tip We have used this method with considerable satisfaction for several years Its disadvantages we found were chiefly that the larger sizes were unwieldy and that sterilization of the catheters

TABLE I—BILIARY TRACT OPERATIONS

1931 1934, Inclusive, at Massachusetts General Hospital

	[illegible]		[illegible]		[illegible]		[illegible]	
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Total operations for biliary stones	[illegible]		[illegible]		[illegible]		[illegible]	
Common ducts explored	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Common duct stones recorded	[illegible]		[illegible]		[illegible]		[illegible]	
In ducts explored		[illegible]		[illegible]		[illegible]		[illegible]
In all gall-bladder operations				[illegible]		[illegible]		[illegible]

was difficult. The catheters also are expensive and short lived, and when they become roughened with use may damage the tissues through which they pass. Cheever however and many of his pupils have had no fault to find with the method over a period of several years. Many surgeons having realized the importance of dilatation of the papilla in selected cases have used a variety of urethral sounds and bougies for the purpose. The long olive tip bougies with bendable shafts proposed by J Bakeš, of Brueun Czecho-Slovakia, are very satisfactory We have used them in more than 231 instances in our hospital since they were brought to our attention in 1930 by Dr Richard Chute The sizes are graduated from a diameter of 3 millimeters to that of 14 millimeters. Although Bakeš always advocated dilating the outlet of the duct to a size just below that of the duct itself we have rarely used the larger sizes We do think it important to dilate the papilla to a sufficient size to allow stones lodged in the hepatic ducts to pass after operation, and have collected stones in the stools in a few such instances. We have opened the duodenum over the papilla in 7 cases when the probe or small dilator failed to go through from above with ease. In these patients and in experiments on dogs we have been impressed by the minimal damage to the tissues through which these dilators pass. It is probable that in certain cases with large ducts, a constricted outlet, and a damaged liver better results will be obtained if the outlet is dilated to a considerable size, even up to 1 centimeter or more The outlet is likely to remain dilated indefinitely and the bile will then be delivered directly into the intestine. We are sure that this will eliminate prolonged T-tube drainage to the outside in certain cases in which a protracted period of drainage is desired. We feel, however that in the routine case, an average dilatation up to 7 millimeters will suffice. We urge that gentleness and care be taken to direct the probes properly under palpation and under vision. If undue force is necessary we believe it safer to open the duodenum and begin the dilatation in a retrograde fashion. Under no circumstances should dilators as large or larger than the diameter of the duct itself be used since it is not our purpose to stretch the walls of the supraduodenal portion of the duct, but simply to dilate the outlet.

All thoughtful surgeons admit the importance of and most of them practice, the procedure of ascertaining in some manner the patency of the papilla of Vater when the common duct is opened. Without doubt in the majority of cases, this alone will suffice We have been impressed however with the uncertainty of clearing the hepatic ducts of stones or débris Also we believe that the frequency of finding a constriction of the duct outlet justifies dilatation of the papilla in a safe manner and to a suitable degree routinely when we explore the ducts. That this is not a dangerous procedure is borne out by our statistics. Although it appears that the mortality is lower if in duct exploration the papilla is dilated than when it is not (Table II) we believe that this apparent discrepancy may be due to other factors. We are sure that in the hands of a good many operators from chief surgeons to resident staff even when reasonable care is used ample opportunity is offered for serious difficulty with the method if it were dangerous

TABLE II —TOTAL BILIARY TRACT OPERATIONS

Massachusetts General Hospital—October 1, 1930—October 1, 1935

	Cases		Deaths		Percentage of mortality	
Cholecystostomy	82		12		14 5	
Cholecystectomy[1]	751		22		2 9	
Cholecystectomy with common duct exploration and dilatation of sphincter[1]	231	395	9	17	3 9	4 4
Cholecystectomy with common duct exploration and sphincter not dilated[1]	164		8		4 9	
Total (5 years)	1228		51		4 2	

[1]Under the headings "Cholecystectomy with common duct exploration" are included several cases of secondary choledochostomy, the gall bladder having been removed at a previous operation

External drainage of the common duct has been the practice of choice although a few surgeons have advocated internal drainage through the papilla The reasons for outside drainage temporarily, in addition to dilatation of the duct outlet, are that we are certain that tight closure of the duct incision is difficult to obtain and a temporary reaction with swelling at the papilla after dilatation may exist It is likely that the hydraulic action in a tightly closed duct would be more effective in discharging stones overlooked, but this is offset by the advantages of taking the pressure off the duct suture line as well as of relieving the liver of any temporary resistance to the flow of bile If drainage from the abdominal cavity alone is depended on to take care of the bile that escapes from the incision in the duct, the bile is delivered into the abdomen faster than the drains can accept it, thus causing bile peritonitis, which, although rarely fatal, in all cases, retards convalescence In no instance have we had cause to regret the use of the small catheter in the duct, which drains approximately 400 cubic centimeters daily or about one-fourth of the average daily secretion of the liver It gives us some indication of the activity of the liver, and in rare instances, valuable information concerning the patency of the duct outlet This catheter is sutured with No o chromic catgut into the duct and removed with the wick on the tenth or twelfth day The stab drainage wound is dry by the fifteenth day, and in no instance have we had to re-establish drainage in the sinus

TABLE III —CAUSES OF DEATHS IN BILIARY TRACT OPERATIONS

Massachusetts General Hospital—October 1, 1930—October 1, 1935

	Cases		Cases
Pneumonia	12	Shock	1
Pulmonary emboli	9	Subdiaphragmatic abscess with rupture into pericardium	1
Peritonitis	9	Cholangitis	1
Pancreatitis	7	Bilateral pulmonary collapse	1
Hemorrhage	5	Pulmonary edema	1
Bile peritonitis	2		
Liver death	1		
Myocardial failure	1		

POSSIBLE COMPLICATIONS FROM DILATATION OF THE PAPILLA

The dangers that might arise in the routine instrumental dilatation of the papilla of Vater when the common duct is explored materially have occurred to us We approached the method with great caution thinking particularly of the possibility of duodenal reflux In only one instance has this occurred, and that we feel sure was due either to a false passage of the catheter into the duodenum or to the placement of the catheter through the dilated papilla into the duodenum Duodenal contents came through the catheter while bile was delivered through the cigarette wick This patient made a good recovery and all drainage ceased on the twenty-first day One of the other dangers we considered, was cicatricial constriction of the dilated duct outlet We have seen no evidence of this condition in the 231 cases so treated So far, 2 patients have returned for secondary operations

CASE 1 A patient who had a cholecystectomy for gall stones and stones removed from a dilated common duct with dilatation of the outlet to 1 centimeter in the presence of jaundice, returned 3½ years later with jaundice following colic At the second operation a large stone was removed from the ampulla of Vater, after which the 8 millimeter dilator passed into the duodenum with ease

This indicates that stones may form in the common duct in spite of a dilated outlet

CASE 2 The other patient was operated upon in October, 1934, after a 6 weeks' history of pain, jaundice, and chills His gall bladder was thick walled and chronically inflamed but contained no stones It was removed and a large duct was explored but no stones found The outlet was found constricted and was dilated to 9 millimeters This patient drained

an abnormal amount of bile through his catheter the amount reaching 2,500 cubic centimeters in one 24 hour period. After the catheter was removed on the tenth day he had a severe attack of colic, which we interpreted as due to the passage of an overlooked calculus. He made a rapid recovery afterward, but several months later began having a return of symptoms and finally became jaundiced. He naturally was hesitant about a second operation but after a severe intestinal hemorrhage, he finally returned to the hospital. At operation this time, the duct was found dilated and much thickened and no instrument would pass through the outlet. His condition did not permit further maneuvers at the time, so the duct and abdominal wounds were drained. A reasonable amount of very thin bile was obtained daily administered in the form of cocktails or through a nasal tube for several days. In spite of this, his appetite failed and his condition became precarious with low blood chlorides and low serum protein, associated with a rising non protein nitrogen. A jejunostomy was performed to permit feeding, 19 days after the choledochostomy. Since this procedure, he has gradually gained in strength and the character of the bile draining from the sinus has improved. His appetite has returned so that the jejunostomy is now used for the replacement of bile only. We believe that he will gain sufficiently to permit a future operation to re-establish the bile drainage into his duodenum.

There has been only one other possible complication following dilatation of the papilla. In this case, the operator stated that there was no evidence of pancreatitis at the time of cholecystectomy and exploration of the duct. The outlet was dilated to 8 millimeters in the presence of a dilated duct from which stones had been removed. The patient developed acute hemorrhagic pancreatitis from which she died 3 weeks later. Whether the dilatation played a rôle in the pancreatitis is a matter of conjecture, but it must be considered as a possibility. Recently however we have purposely dilated the papilla in the presence of fat necrosis recovery was comparable to that after routine cholecystectomy and far more quickly than the average in the presence of acute pancreatitis. It is only fair to state that Lahey has recently reported 2 cases of fatal gas bacillus infection following the instrumental dilatation of the papilla of Vater. We do not believe that this unfortunate complication was brought about by the dilatation. We all know that the gas bacillus may be found in the gastro-intestinal tract or even in the gall bladder itself. Fortunately this type of contamination is rare and none of us hesitate, when necessary to open the duodenum or jejunum in a comparatively unaseptic manner.

STATISTICAL DATA

In the 5 year period from October 1930, to October 1935 1,228 patients with biliary tract disease have been operated upon at the Massachusetts General Hospital. Of these, 395 or 32 per cent have had the ducts explored. Stones removed from the ducts were recorded in 167 patients representing 42.2 per cent of the ducts explored and 13.6 per cent of the total operations. Fifty-one patients died a mortality in the whole group of 4.15 per cent. In the 395 who had duct explorations, 17 died a mortality of 4.4 per cent. When we consider that the highest mortality (Table II) occurred in those patients considered too ill to have more than cholecystostomy done, it may seem to offset the apparent lack of increased danger in duct exploration as compared to the mortality of 2.9 per cent in simple cholecystectomy. We must consider however that the duct explorations included many secondary operations (61 cases) and also the very poor risk patients with prolonged jaundice. On the whole we feel justified in stating that choledochostomy superimposed upon cholecystectomy if carefully carried out, increases the risk slightly if at all. One hundred forty five, or 42 per cent, of the duct operations were in patients without history of jaundice. In this group stones were recorded in 49, or 34 per cent. A history of frequent attacks was given in 273 cases. 223 had enlarged ducts, 98 had chills and fever, 61 had had previous biliary tract surgery and 46 had pancreatic disease.

SUMMARY

1. We urge that common duct exploration be carried out in primary operations on the biliary system when the history or operative findings suggest the possibility of stone within the ducts or a constriction of the duct outlet.

2. We feel that routine instrumental dilatation of the papilla of Vater is not only a logical but a safe procedure in all ducts explored.

3 We advocate temporary drainage of the bile duct to the outside and drainage of the abdominal cavity

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Discussion

DR. STANLEY H MENTZER, San Francisco The wisdom of exploring the common duct more frequently during the course of operations upon the gall bladder is shown admirably by Dr Allen Past experience and present practices have justified the slightly increased risks that this new treatment entails, for the end-results are better and re-operations are less frequent.

Dr Allen repeatedly urges that care and gentleness be maintained during the dilatations of the sphincter of Oddi Those who have seen the esophagus, ureter, and rectum split by similar mechanical dilators, appreciate the necessity for care and they will respect the teachings of the author But the surgeon less experienced in the necropsy room may not be cautioned by his past training Under these circumstances, the dilatations advocated by Dr Allen are fraught with potential harm The sizes of the larger dilators are enormous in respect to the anatomy of the normal common duct When the common duct is dilated and the largest bougies used, the elastic and muscle tissue of the ampulla of Vater is already stretched, and the danger of rupture of these attenuated structures is therefore increased Although Dr Allen and his associates have not had any complications from the use of this method, it behooves those of us who are less experienced, or not experienced at all, to approach this technique with delicate fingers and tender consideration for pathological tissue

ISCHEMIC CONTRACTURE[1]

ARTHUR STEINDLER, M.D., F.A.C.S., IOWA CITY, IOWA

IN the ill repute which fracture of the elbow enjoys among the medical profession, the ischemic contracture has its full share as one of the dreaded complications. Volkmann, after whom the contracture is named considered it a postmortem rigidity of the muscles strictly due to arterial ischemia and to the complete shutting off of oxygen supply. It was Bardenheuer who later pointed out the importance of the venous backflow stating that the deep venous system, richly supplied with valves has ample communication with the subcutaneous network in the elbow fold by means of an avalvular system of anastomosis which permits the emptying of the deep veins into the superficial ones. This emptying is impeded as the pressure is raised in the layers with a resulting excessive carbon dioxide accumulation in the vein. The endothelial wall becomes damaged and permeation of plasma into the muscles takes place, which finally leads to the well known pathological changes. Defined from the purely pathological point of view ischemic contracture is a fibrous retraction of the muscles of the forearm.

Investigators acutely interested in the causation of this severe interstitial myositis have tried to solve the problem from the clinical as well as from the experimental angle. Is it the shutting off of the blood supply by injury or rupture of the brachial artery or is it due to the subfascial pressure impeding the venous backflow is it caused by involvement of the peripheral nerves, or is it the result of sympathetic nerve lesion leading to vasomotor disturbances?

ARTERIAL OCCLUSION

There is accumulative evidence that arterial occlusion may lead to ischemic contracture. Jones recently reports a number of cases in which the brachial artery was either hooked over the end of the proximal fragment or caught in the fragment where the radial artery was torn where a thrombus obliterated the artery and finally where the artery was occluded by fascial pressure. That ischemic contracture follows immediately upon cessation of the arterial blood supply was also proved by an experiment on a patient of temporarily clamping the brachial artery.

Leriche also called attention to the frequent occlusion of the trunk of the arteries in Volkmann's contracture and Lance in 1933 reports a case of complete obliteration treated with humeral or with brachial arteriectomy. The artery is found completely obliterated by proliferating endarteritis. There is no indication of a primary arterial thrombus but rather a leucocytic infiltration of the media indicating an inflammatory and proliferating process. The arterial occlusion leads to necrotization of the muscles and peculiarly enough, is limited to the flexors and pronators of the forearm.

On the other hand, similar clinical observations are made in venous stasis. Brooks examining the effects of acute venous obstruction, found swelling, muscle paralysis, and blood extravasation into the muscle with polynuclear infiltration and proliferation of the connective tissue.

So far as significance of primary nerve involvement is concerned, opinions are divided. Some observers maintain that the integrity of the peripheral nerve supply is essential for the contracture they find that, after resection of the posterior roots and plaster fixation, the contracture developed slowly and more as a muscle contraction whereas without resection of the posterior roots rapid contracture developed. This would indicate, according to Meyer and Spiegel, that for the ischemic contracture the fixation reflex is necessary the reflex being the primary condition and the muscular contracture the effect.

As a matter of fact, the direct injury to the nerve frequently does occur but it has not been proved as yet that such injury is the primary cause of the ischemic contracture (Jepson). On the other hand it is claimed

[1] Presented before the Clinical Congress of the American College of Surgeons, San Francisco, October 28-November 1, 1935.

that the constriction lasting for a long time, sufficient to close the larger blood vessels of the brachial region, must exert a strong pressure upon the median and ulnar nerves, causing neuritis and degeneration The musculospiral nerve is too deeply placed and too well protected, but the median nerve and in particular the ulnar nerve are frequently involved Again, Leriche and his followers attribute great significance to the irritation of sympathetic nerve supply of the vessels, resulting in peripheral vasoconstriction

In view of these discrepant clinical observations, it should be interesting to review shortly the results of experimentation on the pathogenesis of this contracture

THE EFFECT OF ARTERIAL ISCHEMIA

Meyerding, in 1930, stated that in animals contracture is not produced by the ligation of the artery alone Thrombosis and ligation in either upper or lower extremity results in flaccid paralysis with or without gangrene according to Raffele and Jepson

Stenson ligated the abdominal aorta and likewise obtained flaccid paralysis In a case of our own experience where the femoral artery was ligated for uncontrollable bleeding in a child suffering from osteomyelitis, the result was also permanent flaccid paralysis but no contracture The accompanying sensory paralysis at first complete, gradually receded, but no contracture developed Similarly, the ligation of the external iliac and epigastric, carried out by Lapinski, produced coldness, flaccid paralysis and disappearance of reflex excitability, but no contracture and no muscular rigidity, although histological examination showed changes in muscles and nerves, particularly in the latter, in the form of fragmentation and degeneration

Brooks, in 1925, observed that ligation of the artery alone did not produce total paralysis, and in some instances he could demonstrate fields of totally viable and others of totally necrotic muscle adjacent to each other

THE EFFECT OF BOTH ARTERIAL AND VENOUS OBSTRUCTION

Experiments in which arterial ischemia was used with venous stasis by ligating femoral artery and vein showed contraction phenomena, but these also were transitory, although when ligation was sufficiently high, for instance at the common iliac, gangrene resulted

THE EFFECT OF VENOUS STASIS ALONE

Jepson produced in animals a claw hand contracture by applying a rubber bandage, but this contracture disappeared within 3 to 4 hours after the tourniquet was removed When the femoral vein was ligated, the extremity became cold and bleached and flaccid, and soon went into a claw deformity, the deformity persisting from 6 to 9 days On the other hand, Raffele, after ligating the femoral vein, was not successful in producing a true ischemic contracture

On the whole, the most definite experimental results were obtained where constriction was combined with fixation after fracture of the limb (Raffele) The circulatory disturbance was accompanied by flexion rigidity and then by contracture which approached the ischemic type In this he probably approached closest the actual clinical condition, since there was added a hematoma in the subfascial space of the forearm with diffusion of blood and the subsequent organization

In view of the fact that Volkmann, and in fact others, maintain that the circulatory obstruction is responsible for this deformity it is interesting to note the difficulties with which ischemic contracture is produced experimentally In fact, Serra goes so far as to say that in the light of experimental investigations the plaster cast is almost completely exonerated, a statement which, I believe, is somewhat overdrawn

Our own statistics, based on 50 cases, show that casts were applied in 18 cases, splints were applied in 18 cases, the Velpeau bandage in 8 cases, the acute angle or right angle position was assumed in 26 cases, position not stated but presumably right or acute angle, 30 cases No immobilization was applied in 4 cases Since among the total number, only 18 patients were treated by plaster cast, one may wonder whether in general the plaster bandage can be accorded a prominent rôle in the production of ischemic contracture While a constricting dressing may easily accentuate

the effect of the trauma by preventing the establishment of collateral circulation. It certainly cannot unconditionally be held responsible for the development of this deformity. On the other hand the cast or bandage can be a very definite contributory cause and for this reason, careful supervision and general vigilance are essential features in the treatment of this fracture. But, I believe there are other factors of even greater importance in regard to medical responsibility.

PREMONITORY SIGNS AND THEIR SEQUENCE

In general one may state that the sequence is coldness, cyanosis, swelling, paresthesia, pain, flaccid paralysis, contracture of the flexor muscles and, finally, the development of the claw hand, *main en griffe*. But there is a considerable difference in the rapidity in which the events follow each other also in the time of latency and finally in the intervals between the first premonitory symptoms and the development of definite objective symptoms. In our own series acute premonitory symptoms were observed in 35 cases in 10 of these immediately, in 8 within the first week, in 10 after the first week, in 7 cases later. In 15 cases no data of acute signs such as cyanosis, numbness, or paresthesia were given.

In 20 cases in which definite statements of acute symptoms and their time of onset were at hand, the timely removal of the dressing that is at the first appearance of the symptoms was recorded 6 times while the late removal of the dressing after an undue interval following the acute premonitory symptoms, was recorded in another 14 cases. Among 15 cases on the other hand, in which no acute symptoms occurred timely removal of the dressing, that is upon the first sign of contracture, was recorded in 10 cases and delayed removal in only 5. In 7 cases the contracture developed while the cast was being worn while in the majority the contracture did not appear until after removal of the cast.

It would appear from this short analysis that if any accountability exists, its particular burden lies in the failure to pay proper attention to the first premonitory signs and not so much in recognizing the actual beginning of the contracture.

PATHOLOGY

Corresponding to these two clinical stages the acute premonitory signs and the chronic development of contracture there can be distinguished two pathological phases. The first is characterized by edema, cyanosis, the waterlogging of the perimysium of the muscles, the infiltration and accumulation of leucocytes in the interfibrillary spaces, loss of the nuclei of the sarcolemma, loss of transverse and longitudinal striation, the irregularity of contour, undulation and finally the defibrillation and separation of the individual muscle fibers ("myolysis," Marenesco) leading to atrophy and fragmentation of the muscle fibers. The muscle degeneration is of the granular type, there is no fatty degeneration and there is also no intermuscular hemorrhage.

In the second stage there is a gradual absorption and destruction of the disintegrated muscle fibers. Rafele calls attention to special cells arranged circularly around the muscle fibers particularly near the vessels, in immediate contact with the muscle fibers. They penetrate the fibers and absorb their contents. They are histolytic cells of local origin with purely phagocytic function. One can also see pigmentation and round cell infiltration of the muscle fibrillæ. It finally comes to a substitution of the destroyed muscle fibers by fibrous tissue from the surrounding connective tissue elements. Peculiarly enough, the pathological changes are rather unequally distributed, and one finds some portions of normal or almost normal muscle elements preserved while others have completely succumbed to fibrosis.

Vessels and nerves are found embedded and constricted in fibrous masses. Myositis ossificans in ischemic contracture is described by Nitsche as probably due to the hematoma which, poorly absorbed produced not only connective tissue proliferation but was also responsible for the ossification which occurred 4 months after the injury.

THE CLINICAL PATHOLOGY OF THE CONTRACTURE

Acute stage. The acute prodromal symptoms last only 1 to 2 weeks and they are in sequence edema, cyanosis, pain, paresthesia,

hypesthesia, motor paralysis, and trophic disturbances Among our 50 cases we found numbness as initial symptom in 26 cases, edema in 12 cases, cyanosis in 5 cases, trophic disturbances in 12 cases

Permanent stage The muscles first become flaccid, then there is muscle rigidity, and, according to Jepson, after 65 to 70 hours, the muscle is again flaccid and tender to pressure After 2 weeks, the swelling disappears and the formation of the contracture begins

Of interest is the almost exclusive localization of the contracture in the flexor and pronator groups of the forearm This is explained by Soubeyran (1922) by the peculiar anatomy of the arterial system of the arm, the circulation stopping at the ventral part but being secured dorsally by numerous anastomoses The contracture is a combination of flexion of the mid-phalanx and end-phalanx with flexion of the wrist To this is added the extension contracture of the metacarpophalangeal joints and the pronation contracture of the forearm Although this is the most frequent type of contracture, it is by no means the only one In many cases, the hyperextension contracture of the metacarpophalangeal joints is missing, and others only show a flexion contracture of the wrist similar to that seen in musculospiral palsy The abduction of the thumb is another feature The thumb is held in the plane of the fingers, having lost its power of opposition and pronation against the palm It is often associated with strong flexion of the end-phalanx of the thumb due to contraction of the long flexor In the fully developed claw hand contracture, the pathological sequence of contracture can be readily understood First, there appears the flexion of the finger joints, then follows the flexion of the wrist, and later follows the extension contracture of the metacarpophalangeal articulation with retraction of the knuckles The hyperextension of the metacarpophalangeal articulation is largely the result of the passive insufficiency of the extensor group, but does not necessarily indicate that there is loss of action of the interosseous muscles

It is somewhat different if there is a secondary peripheral nerve involvement Then the claw hand deformity becomes somewhat modified, depending upon the contributory effect of the nerve lesion If there is ulnar nerve involvement, the claw hand formation becomes much more accentuated

Sensory lesions We found sensory lesions, on the whole, rather frequent complications, but in the majority of these cases the disturbances are not anatomically defined, as one would expect when a peripheral nerve trunk is injured There is, as a rule, an area of hypesthesia with a hyperesthetic border, but it is not uncommon to see the hypesthetic area recede after correction The unanatomical distribution of the sensory loss denotes rather a circulatory disturbance than a direct lesion of the peripheral nerves In some cases in which the anesthesia is anatomically defined, we may assume that a primary nerve lesion exists, and this is more often found in the territory of the ulnar nerve

Trophic lesions appear, as a rule, in the more severe cases with sensory and vasomotor changes They range from the dry cold skin, dry striated nails, and atrophy of the subcutaneous tissue, to ulcerations of the knuckles Here, also, one often sees that the trophic lesions rapidly heal after correction of the deformity is accomplished Ordinarily, however, all the traces of acute symptoms as well as the trophic and circulatory lesions have disappeared by the time the contracture develops So we found trophic lesions present at the time of examination in only 1 case, although many cases had scars from trophic ulcers which occurred at early stages Sensory lesions persisting throughout the contracture stage were observed in anatomical distribution in 7 cases, and in non-anatomical distribution in 11 Circulatory disturbances persisting into the chronic stage were found in 5 cases, while 22 cases showed none of the primary prodromal symptoms which characterized the acute stage

On the whole, one may distinguish two types of ischemic contracture In the first, there is a precocious and simultaneous appearance of acute symptoms and functional disability In the second type, there is an early development of acute symptoms which run their cycle of development and disappearance and which can be considerably modi-

fied by the prompt removal of the dressing. In cases in which the acute symptoms have already disappeared at the time the retraction begins, examination shows merely the signs of the chronic stage usually the typical claw hand with some infiltration of the skin, possibly a diminution of the radial pulse, and sometimes a persistent segmentary distribution of sensory changes which is due to secondary peripheral nerve involvement by the retracting muscle tissues.

TREATMENT

The most important phase of the treatment is the prophylaxis. First of all, there is the reduction of the fracture or dislocation itself in good apposition and the maintenance of correction second in importance is the position chosen for immobilization. Of the 50 cases, immediate and successful reduction was accomplished in 31 cases, and unsuccessful or late reduction in 5. It appears, therefore, that immediate and successful reduction in itself does not materially influence the incidence of ischemic contracture.

Another question is whether the incidence of contracture is lessened if plaster or metal splints are used instead of circular casts. From our own analysis, it appears doubtful that much blame can be placed upon the circular dressing as such provided a good plaster technique is used. It seems more to the point that prophylactic measures should be directed against the primary position which in the majority of cases was that of acute or right angle flexion. J. B. Murphy in 1914 pointed out that prophylactic treatment consists in avoidance of compressive splints and bandages and in permitting a position of greatest comfort for the first 48 hours, never a flexed position immediately after the accident.

The treatment of the contracture. On the whole, conservatism should be the pass word for the treatment of the contracture in all its elements. The treatment of Robert Jones is generally recognized as paramount. It is admirably described in his article on "Volkmann's Ischemic Contracture" in the *British Medical Journal* 1928. Since 1908 he has advocated gradual extension first of the fingers, then of the metacarpophalangeal joints and lastly of the wrist. When the wrist is completely flexed the contractures of the fingers are lessened, and if they cannot be fully extended, they may be further straightened by completely flexing the metacarpophalangeal joints. When the fingers are straight splints are applied to them and they are used to extend the metacarpophalangeal range. Then splints are applied reaching from the finger tips to the wrist joint and, finally full extension of the hand is secured the splints being used as levers to dorsiflex the wrist slowly. The splints should be taken off every day for the application of physiotherapeutic methods consisting in several modalities of thermotherapy the most useful of which is diathermy as it promotes best nutritive stimulation. This is assisted by mechanotherapy and massage the former consisting in passive mobilization directed separately against the capsular contractures which develop in the metacarpophalangeal joints as well as in the interphalangeal articulation and against the flexion contracture of the wrist and the pronation contracture of the forearm.

Rapid redressment of the deformity as advocated by Volkmann, Koenig, Hildebrand, and others, is on the whole unsatisfactory. It produces lacerations and invites recurrences. The gradual and slower redressment, however as used by Froehlich, Putti, and others, by a series of corrective splints or casts, is a very effective method. On the whole, the gradual correction is better accomplished by splints in the manner indicated by Robert Jones. Instead of the rigid splint, one may use the semirigid wire splint of Ombredanne and others, or the hinged splint of the type used by Alexander Rowland, etc.

One of the most efficient methods of gradual correction is that of elastic traction. It may be carried out by spring extension such as in Putti's splint or in the splint models of von Recklinghausen or by means of a glove traction splint as used in our clinic or as the banjo splint which obtains correction by elastic traction of the fingers against the so called banjo frame. Another very useful and practical type of splint is the so called Quengel splint, devised and perfected by Mommsen.

OPERATIVE METHODS

That operative methods in the treatment of ischemic contracture are contingent upon the failure of the conservative treatment to accomplish results is generally agreed upon, and needs no further mention The question is, however, what constitutes failure, or to put it in other terms, when is it reasonable to expect the conservative method to have reached its limit? The contracture resistance is very different in the muscles of the different joints of the extremities The short fibered, uniarticular muscles of the wrist joint are very much more resistant in contracture than are the muscles of the fingers, which have a very much wider contraction range because of the greater length of the muscle fibers Aside from the purely anatomical aspect of morphological variations in the make-up of the different muscles, it should be remembered next that the ischemic contractures are in all respects different from contractures seen in spastic paralysis or in attitudinal contractures It is not a contraction, it is a passive state, and it can be shown that contracture is maintained at a minimum of oxygen expenditure, in which respect it materially differs from all active contraction It is due to the physical nature of this contraction that for its correction continuous and steady counterforces are required, because the resistance to correction increases rather than decreases with the improvement of position—in wide contrast with contractures seen in spastic or positional conditions

While all contractured muscles resist gradual mechanical stretching, the flexor carpi ulnaris offers by far the most difficulties Because of its comparatively large rotation, the moment the deformity yields to mechanical pull and flexion, ulnar deviations are produced One should not hesitate to lengthen this muscle by tenoplasty, this also applies to the flexor carpi radialis These muscles were severed in the majority of cases

Another muscle which offers strong resistance is the deep flexor pollicis longus This muscle coming from the ulnar side of the radius and interosseous membrane, has a comparatively short contraction range With these three muscles, the usual obstacles to correction are overcome, and it is only very rarely necessary to lengthen the long muscles of the fingers These muscles have a much larger contraction range and consequently yield much better to stretching

Transverse myotomies generally are not to be recommended except for the pronator teres and pronator quadratus, they mean as a rule, a total sacrifice of the muscle

Stripping the flexor group off its point of origin at the internal epicondyle of the humerus is a method already advocated by Bardenheuer and Codivilla It produces a release of the flexion contracture of the wrist, but the detachment is possible only for a short distance, ½ to ¾ inch, because of the innervation by the branches of the median nerve

Tendon transplantations in ischemic contracture, especially transplantation from the extensor to the flexor muscles, are indicated in cases in which there is a great deal of myositic destruction Such operation, of course, presupposes surgical removal of the scar tissue In our cases, myotomies of the pronators were carried out in 4 instances, epicondylar stripping in 5 cases, tendon transplantations in 4 cases, conservative method of plastic lengthening confined to the wrist flexors in 27 cases, tendon transplantation using flexor carpi radialis and ulnaris for the flexors in 2 cases

Operations on bone Although operations on the skeleton are carried out infrequently, they may be the only suitable procedures in the severest deformities The resection of the radius and ulna which was first carried out by Colzi in 1892, we have used in only 1 case, because of the uncertainty of the method and the possibility of radio-ulnar synosteosis Usually we prefer the method of resection of the wrist when it is necessary to shorten the skeleton, in order to accommodate the irresistibly contracted flexor musculature

Pouzet advocates the partial resection of the carpus, preferring it to resection of the forearm bones, as being more simple, more sure, having a better cosmetic result, and offering a better control of the ulnar deviation The resection of the distal row of the carpus was first proposed by Phocas in 1911, later it was carried out by Klapp and others

On the other hand, it is not infrequently necessary to resort to radical operations in

severe claw hands with subluxations or dislocations of the basal phalanges on the heads of the metacarpals. In these cases it is usually not sufficient to resort to capsular stripping. One must often resect the metacarpal heads, since a claw hand of that degree is not manageable in any other way The resection of the metacarpal heads was carried out in 1 case.

Operations on nerves Neurolysis is recommended in those cases in which a primary involvement of the ulnar and median nerves appears likely that is in more or less anatomical distribution. At operation one may find anything from a few constrictions of the nerve to scar tissue and complete strangulation. Occasionally neurolysis should be combined with transposition of the ulnar nerve.

The question of the effect of surgery upon the circulatory aspect of ischemic contracture needs further discussion. Leriche is a principal advocate of arterial surgery and reports of Matthieu and others on arteriectomy of the brachial artery seem to indicate that some improvement in regard to certain aspects of the deformity can be expected. Putti also has reported good results from this method. On the other hand, we find nothing in the literature regarding the effects of ramisection in ischemic contracture.

In our series, neurolysis was carried out in 2 cases with good results and neurolysis of the ulnar nerve with transposition was performed in 2 other cases. A skin graft was necessary in 1 case to cover a scar caused by trophic ulcers.

The mechanical after treatment both in conservative and operative management is so generally emphasized that it is not necessary to say more. It is the backbone of the treatment and there is no complete or lasting result without it A single massage and mechanotherapy sitting need not exceed 15 or 20 minutes for the extremity It should be preceded by the application of radiant heat, whirlpool or paraffin bath. The massage should be followed then by passive motion and the application of splints We believe also that active motion of the hand may be carried out with great advantage under water Graphic records should be made both of position and range of motion in order to follow up the effect of the treatment.

It should be borne in mind that the restoration of form, accomplished by conservative and operative methods and followed by mechanical measures, is only one side of the treatment. Restoration of function is the other and this depends largely upon muscle reeducation. It is a matter of rather prolonged training and drill. Under these conditions the treatment of more severe cases may easily occupy 1 year or longer while the more favorable cases may show definite results after a period of 6 months.

END-RESULTS

In a series of 50 cases of ischemic contracture, 43 were treated Eleven cases were treated conservatively only of these 4 showed good results 1 fair 1 poor and 5 undetermined. Thirty-two cases were treated by operation of these 8 were good 8 fair 4 poor and 12 undetermined.

In presenting this summary of end-results, it is hardly exact to compare the achievement of the treatment without due regard for the difficulties offered by the individual case. Sometimes a moderate end-result in a desperate case is more of an accomplishment than a brilliant correction in a mild deformity But in nearly all cases we are confronted with a problem of reconstruction involving many therapeutic phases, and not with a single corrective maneuver All in all, this deformity offers great possibilities for rehabilitation under well laid plans.

THE IODINE RELATIONSHIPS OF THYROID DISEASE[1]

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THAT iodine is of consequence in the investigation of thyroid disease long has been a matter of common knowledge The thyroid gland is a principal storehouse for iodine, the thyroid hormone has a high iodine content, and the use of iodine in the prevention and treatment of goiter is household conversation Nevertheless, during the past decade, newer facts have been added to the iodine story It is now established that iodine is constantly present in human blood *Presumably* a part of this is actually circulating thyroid hormone There also occurs a constant daily loss of iodine in the urine The level of the blood iodine fluctuates, likewise the daily excretion of iodine in the urine There is prophetic significance to these newer facts when applied to the problem of thyroid disease

HISTORICAL SKETCH

Fortunate indeed was the empiricism which led to the ancient use of burnt sponge in the treatment of goiter Iodine was unknown Its actual discovery came later and then accidentally by Courtois in 1811 when it was revealed a by-product in the preparation of war materials for one of the Napoleonic wars Within a few years Sir Humphrey Davy isolated iodine from sponges, seaweed, and other forms of marine life

This is not the time or place to tell the story of the subsequent century of clinical iodine research extending from Straub, of Berne, to Plummer, of Rochester It must suffice to sketch, if ever so briefly, certain of the highlights of this hundred years of fruitful investigation, in order that a background may be set for present trends and progress

As early as 1831 Boussingault made one of the first endemicological studies in the goitrous regions of the Andes This study demonstrated a significant relationship between iodine and goiter Subsequent investigation led, in 1849, to Prevost's theory which related iodine deficiency to the incidence of goiter This fundamental theory was soon substantiated by the numerous iodine analyses made by Chatin However, while Chatin's work (1850-1876) was recognized, it was not at the time generally appreciated The analytical method which he used was difficult, and contemporary chemists were unable to duplicate his findings

Following the unsuccessful French experiment in 1860, the significance of iodine as related to thyroid disease received a setback During the ensuing 35 years, other theories arose concerning the nature of goiter It was during this period that the infection theory gained credence This was doubtless due to the contemporary discoveries of Pasteur

A number of unsuccessful attempts had been made to demonstrate the presence of iodine within the thyroid gland One of these was in Kocher's clinic at Berne In 1895 Baumann succeeded in isolating considerable quantities of iodine from normal thyroid glands This he demonstrated to his colleagues in its characteristic violet vapor form in tubes It is of particular interest to us that this investigation was suggested to him by Kraske, at that time professor of surgery at Freiburg The significance of the discovery was quickly and widely appreciated

Twenty-four years later Kendall succeeded in isolating thyroxine The isolation was repeated by Harington, who later determined the correct molecular structure Working from this formula, Harington synthesized thyroxine Natural or synthetic, thyroxine is two-thirds iodine Owing to the high iodine content of the thyroid hormone, the intake, circulation, distribution, and excretion of iodine were then more carefully considered In brief, the metabolism of iodine was investigated Advances soon followed

METHODS

To investigate iodine metabolism necessitated the development of analytical methods sufficiently sensitive, yet at the same time sufficiently accurate, to determine truly minute amounts of iodine The iodine content

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of the thyroid gland is comparatively high, hence it had long been readily determined by the older coarser quantitative methods. The usual iodine content of the blood urine and tissues, however is so minute that it was not even detected by the usual available methods. This difficulty was soon answered. In 1923 von Fellenberg at the request of the Swiss Government devised an adequate method for the microdetermination of iodine as it occurs in nature. To accomplish this he perfected and eventually synthesized principles from other known existing quantitative procedures. His micromethod will determine 0 0001 milligram (one ten thousandth of a milligram) of iodine. This method has been extensively applied. By it von Fellenberg, and particularly his pupils Sturm and Lunde have opened a new approach to the relation between iodine and thyroid function in health and in disease Von Fellenberg's wide and convincing studies made 75 years after the pioneer work of Chatin and other investigators, have given a belated confirmation to their pioneer work

During the past 6 years a group of us—Davis, Cole Phillips, Barron Matthews and Puppel—for whom I act as spokesman have investigated extensively various features of iodine metabolism. We have studied experimental animals normal people ambulatory and hospital patients and over 250 patients with various thyroid diseases. For determining the iodine we used first a micromethod devised by Davis and later one further perfected by Phillips Both are essentially developments of the original von Fellenberg procedure. Our experience amounts now to more than 6 000 iodine determinations It is difficult adequately to cover any save the highlights of this material However I wish to discuss certain features of three iodine relationships of thyroid disease These concern, first the iodine of the thyroid gland second the iodine content of the blood and third the loss of iodine in the urine

THYROID GLAND IODINE

The normal human thyroid gland ordinarily contains about 10 milligrams of iodine (Remington) at a concentration of 40 milligrams per cent wet weight. This is found principally in the colloid (Van Dyke) There is a geographic variation in the iodine content the higher amounts being found in glands of inhabitants in oceanic cities. In glands from districts where goiter is severely endemic, as in certain parts of Switzerland the thyroid iodine is decreased There is likewise a seasonal variation Iodine appears to be stored during the summer since the gland content is highest during this period. An ebb ensues during the fall during the winter the thyroid iodine is at its lowest level, averaging about 8 milligrams. This cyclic fluctuation in iodine storage corresponds to the blood iodine level, which is lowest during the winter months (Sturm, 33)

In patients with genuine exophthalmic goiter the thyroid iodine is decreased. It may be as low as 3 milligrams. This was originally recognized by Baumann and has since been amply confirmed. The associated absence of colloid in the hyperplastic alveoli is generally recognized This particular loss of iodine from the diffuse hyperplastic thyroid is one of the iodine deficiency features of exophthalmic goiter

Subsequent to iodization a phase of iodine storage ensues. In this manner iodine therapy replaces the deficiency and the hyperplastic alveoli fill with colloid The thyroid iodine increases and becomes considerably greater than normal. During this period the blood iodine is greatly increased However the alcohol insoluble portion, presumably the thyroid hormone is decreased (Lunde) This suggests an induced reversal in the polarity of the thyroid cell changing its activity from hypersecretion to storage and initiated by increased iodinization The clinical improvement is well recognized It would appear that the thyroid cells are then storing rather than secreting eventually into the blood stream The iodine content of an excised gland, removed after adequate pre-operative iodinization is uniformly high However there is a variation in the iodine content of different parts of these diffusely enlarged glands

Nodular goiters are more variable in their morphology Hence it is difficult to arrive at any clear conception of the iodine relationships of the differing portions of these glands

in this form of hyperthyroidism Their iodine content is most varied In 1 large goiter, it ranged from 4 to 112 milligrams per cent, dry basis The normal thyroid gland contains about 200 milligrams per cent, dry basis Colloid nodules from diverse portions present great variation in their iodine content

The iodine content of the fluid from cysts is low The hyalin-like substance found in the larger cysts has a low iodine and a high iron content This would indicate its hematogenous origin (von Sinner), since in thyroid colloid, the reverse occurs

BLOOD IODINE

The normal iodine content of human blood is about 12 micrograms per cent (0 012 milligrams per cent) This means that normal blood contains about 120 parts of iodine per billion A microgram, often designated a *gamma*, is one one-thousandth of a milligram It corresponds in gravimetric measurement to the micron of linear measurement Thus the entire iodine content of the human blood stream is ordinarily less than 1 milligram In normal individuals the blood iodine, as determined by Phillips' method, ranges from about 9 to 14 micrograms per cent The range and average is a little lower during the winter months, increasing during the spring and early summer (Nitzescu and Binder) Certain variations of normal physiology, notably menstruation and pregnancy, influence the blood iodine This is increased during early menstruation (Maurer) This newer evidence permits of a more careful analysis of the cyclic correlation between ovarian and thyroid function

By adding alcohol to the blood, the blood iodine may be separated into two fractions (Sturm, 33, Lunde) One of these remains in the coagulum even after repeated subsequent alcohol extractions It is thus alcohol insoluble and is designated, the "organic" fraction The other portion, the "inorganic" fraction, is alcohol soluble The organic fraction is presumably the thyroid hormone (Holst) The inorganic fraction appears to be largely the iodine of nutrition

Although the blood iodine is definitely affected by diseases of the thyroid gland, the majority of patients with other than thyroid diseases reveal a normal blood iodine Thus tuberculosis, fractures, chronic osteomyelitis, chronic arthritis, simple infections, obesity without hypothyroidism, hirsutism, lymphoblastoma, and furunculosis ordinarily cause no change in the blood iodine level In patients with cancer, the blood iodine is within normal range

Certain other diseases, however, are accompanied by changes in the blood iodine That of the neurasthenic may be decreased In the leucemias, both lymphatic and myelogenous, the blood iodine is increased, and the basal metabolic rate is elevated Total thyroidectomy has been of benefit to 2 of our patients

In certain severe infections, in osteitis deformans, in certain patients with hypertension, in hypertensive heart disease, and in certain patients with congestive heart failure, we have observed an increase in the blood iodine The mechanism is not entirely clear Further investigation is necessary Blood should be drawn from these patients for analysis in the postabsorptive state Too, they should not receive iodine in any form, save the normal food and water intake

The blood iodine is as a rule increased in patients with hyperthyroidism In our experience about 10 per cent of the determinations may fall within the higher normal range The average increase, to 27 micrograms per cent is greater in patients with diffuse hyperplastic goiters with or without exophthalmos than in patients with toxic nodular goiters (average of 22 micrograms per cent) There is a seasonal variation in the hyperiodemia of hyperthyroidism which reverses the normal cycle (Breitner) The increase is accentuated by menstruation and by pregnancy Fractional analysis of the hyperiodemia reveals that the increase is principally in the organic fraction (Lunde), which is further evidence of the hyperthyroidism

Subsequent to iodinization with Lugol's solution or for that matter any form of iodinization thus far investigated, there ensues a sharp increase in the hyperiodemia Since this is associated with obvious clinical improvement, as shown by the abatement of the principal symptoms, the findings seem at first

paradoxical. The work of Lunde and his associates, however affords a convincing explanation. The *increase* is principally in the inorganic fraction and is due to the medication while there is a *decrease* in the alcohol insoluble, organic fraction. Thus the circulating thyroid hormone presumably is lessened.

Immediately following thyroidectomy a rise in the blood iodine of non-iodinized patients occurs. So far as I am aware this has not been fractionated. There is usually a fall *in the level following thyroidectomy* on patients treated with Lugol's solution. The blood iodine then remains irregularly increased so long as postoperative iodinization is *continued. The level then depends upon* 2 factors the amount of iodinization, and the time which has elapsed since the last administration.

Subsequent to an adequate thyroidectomy for hyperthyroidism and the cessation of postoperative iodinization, the blood iodine eventually decreases to a low normal level. If the thyroidectomy is inadequate, or if but a single lobectomy is performed, the hyperiodemia persists in varying degree Likewise *in an iodine vacation* either subsequent to iodinization for intercurrent disease or between the stages of a two stage lobectomy the blood iodine is increased. At the beginning of the iodine vacation, high normal values may be found

The blood iodine relationships of toxic nodular goiter are similar to those of exophthalmic goiter We have observed thus far no constant and essential difference

There is no constant and specific correlation between *the blood iodine and the basal metabolic rate* In general both are increased in hyperthyroidism. Thus 11 patients with exophthalmic goiter presented a blood iodine averaging 27 micrograms per cent and a basal metabolic rate averaging plus 50 One of these patients had a blood iodine of 16 and a basal metabolic rate of plus 19 Another presented a blood iodine of 23 and a basal metabolic rate of plus 96. This holds for normal individuals as well as for patients without *thyroid disease.*

Patients with unmedicated hypothyroidism have a decreased blood iodine. This is true for dwarf cretins, for cretins with goiter for children with juvenile myxedema, for adults with a low basal metabolic rate and other evidence of thyroid underfunction, and for *patients with postoperative myxedema.* Perhaps the best evidence we have of the decreased blood iodine in patients with hypothyroidism is that following total thyroidectomy for congestive heart disease there ensues a transient increase in the blood iodine, persisting for about 24 hours. After variable periods, it then progressively *decreases to about one-third normal* averaging 4 micrograms per cent. So far as I am aware, this has not been fractionated. However it is of peculiar interest *in that it corresponds quantitatively to the* inorganic fraction of normal blood (Sturm) It would appear to be due to the iodine of nutrition.

The administration of thyroxine which is 65 per cent iodine, to patients with hypothyroidism is followed by a prompt increase in the blood iodine. This may be great at first. Similar results follow the administration of desiccated thyroid but the subsequent change is not so pronounced however since *dried thyroid (U S P) contains but about* 0 20 per cent of iodine. In patients with hypothyroidism, the continued administration of controlled adequate amounts of desiccated thyroid stabilizes the blood iodine at a high normal level.

In other thyroid diseases the blood iodine varies with the corresponding change in thyroid function. Thus, it was increased in 2 patients with carcinoma of the thyroid, and normal in a third. The absence of specific *correlation* between the blood iodine and the basal metabolic rate is again evident in patients with thyroid cancer

The blood iodine is at a low normal range in patients with *Riedel's struma. In this disease* the extensive sclerosis destroys progressively thyroid alveoli and secreting thyroid cells In 1 patient with struma lymphomatosa (Hashimoto) the blood iodine was within the normal range previous to a partial thyroidectomy Two patients with a median thyroglossal sinus and 1 with a patent thyroglossal fistula presented low blood iodines. Three patients presented, after operation, developing exoph-

thalmos subsequent to adequate subtotal thyroidectomy for diffuse hyperplastic goiter with hyperthyroidism Investigation of their blood iodine and of their basal metabolic rate revealed normal findings Thus no residual hyperthyroidism could be demonstrated by laboratory investigation

URINARY LOSS OF IODINE

It is a well recognized physiological observation that the urinary excretion of crystalloids is closely related to their concentration in the blood As a consequence, we began long ago the investigation of the urinary loss of iodine, particularly in patients with thyroid disease

The daily loss of iodine in the urine of normal individuals, and of University Hospital patients without evidence of thyroid disease, is variable The factor of food iodine intake is inconstant and must be taken into consideration Thus on 4 successive days, the food iodine intake of 1 of our goiter patients was 161, 196, 168, and 207 micrograms The urinary loss of iodine for the same 4 days was 121, 111, 103 and 118 micrograms (Cole, Curtis, and Bone) The food intake of this patient was increased because of pregnancy From 10 to 43 successive determinations made on 10 different individuals gave averages of from 36 to 78 micrograms daily The grand average of over 200 determinations was 55 micrograms Nine of the 10 were maintained upon the usual hospital diet Iodized salt was not used, and sea foods or other foods known to be high in iodine were avoided

Patients maintained for days upon a constant monotonous diet have a remarkably uniform daily loss of iodine in the urine Thus 1 normal male subject under strict hospital control ingested 156 micrograms daily During 4 successive 3 day periods the daily iodine excretion varied from 43 to 53 micrograms, averaging 48 A normal female subject ingested 56 micrograms daily and similarly excreted 36, 36, 36, 31, and 35 micrograms Concerning these patients, there is a considerable daily iodine loss in the stool and sweat (Cole and Curtis)

During certain phases of the disease, patients with hyperthyroidism lose an increased amount of iodine in the urine (Curtis and Phillips) Thus 1 woman with toxic nodular goiter of 4 years' duration excreted from 405 to 628 micrograms daily during a 7 day period The average daily loss was 483 micrograms, approximately nine times normal Her blood iodine varied from 22 to 27 micrograms per cent, and her basal metabolic rate varied from plus 46 to plus 49 during the same period

That an iodine diabetes occurs during the course of hyperthyroidism is demonstrated further in an investigation of 5 patients, women from 27 to 73 years of age, with toxic nodular goiter The basal metabolism varied from plus 18 to plus 69, averaging 43, the blood iodine varied from 15 to 37 micrograms per cent, averaging 22, and the daily loss of iodine in the urine ranged from 139 to 483, averaging 304 micrograms, which is six times normal

Likewise, in 11 patients with diffuse hyperplastic goiter with hyperthyroidism, an increased loss of iodine in the urine was demonstrated Of these, 7 were women and 4 were men, their ages ranging from 17 to 51 Their basal metabolic rates varied from plus 18 to plus 109, averaging plus 69 The blood iodine varied from 14 to 35, averaging 26 micrograms per cent The daily iodine excretion in the urine ranged from 65 to 310 micrograms daily, averaging 157, a threefold normal

Two evidences of iodine deficiency are thus demonstrable in patients with hyperthyroidism (1) the decreased iodine content of the thyroid gland, and (2) the increased loss of iodine in the urine Also certain of our results concerning the loss of iodine in the urine following total thyroidectomy support the hypothesis that there is a loss of iodine from the tissues

Further evidence of the existence of iodine deficiency in patients with hyperthyroidism is shown by their usual response to iodinization, a form of replacement therapy Investigation of the urinary excretion of iodine previous to and following the quantitative administration of 10 milligram doses shows at first but a small percentage excreted in the urine Later, as the depleted thyroid gland and presumably the tissues become repleted, the administered

iodine is more nearly quantitatively excreted in the urine, showing that the deficiency has been overcome. These facts form the basis of an iodine tolerance test, since patients with hyperthyroidism tend to retain iodine administered in small amounts.

In patients with diffuse non-toxic colloid goiters, the urinary iodine loss is normal. Thus, in one woman of 29 it ranged from 36 to 65 averaging 58 during an 8 day period. In a woman of 22 with a non toxic colloid goiter it ranged from 51 to 73 micrograms during a 7 day period.

There is a periodic increase in the urinary excretion of iodine in women during the course of the complete menstrual cycle (Cole and Curtis). Thus 1 woman lost 42 to 53 micrograms daily just previous to the onset of menstruation, 108 to 112 during menstruation and 41 to 65 during the days immediately following. The blood iodine rose to 43 on one of the days of the increased iodine loss. These cyclic variations of iodine loss in the urine appear to be associated with the periodicity of ovarian activity. By investigating the blood and urinary iodine, it would seem possible to correlate more closely thyroid and ovarian function.

An increased urinary loss of iodine also occurs during certain periods in the course of pregnancy (Enright, Cole, and Hitchcock). If iodine deficiency is of major significance in the etiology of goiter, then women should have goiter more frequently than men owing to this periodic and gestational loss.

Subsequent to partial thyroidectomy for the various forms of goiter there is a great increase in the urinary loss of iodine, sometimes as great as 2 milligrams during a 24 hour period. The source of the excess iodine lost has been of interest. Manipulation of the gland during the resection was at first regarded as a likely possibility. Too after resection a certain amount of necrosis follows, and the associated fluid exudate has considerable iodine content, a part of which may be resorbed and excreted. On the other hand an increased urinary loss of iodine follows total thyroidectomy (Curtis and Barron). No raw areas of thyroid gland are left behind in this procedure. Moreover an increased urinary excretion of iodine follows surgery upon remote parts other than thyroid. The loss of iodine from the extrathyroid tissues suggests interesting problems concerning the function of iodine in man, probably iodine has another function in nutrition separate from that of furnishing the high iodine content of the thyroid hormone.

Hyperthyroidism is characterized by a number of salient features. To the original Merseberg triad have been added Chvostek's tremor and certain clinical signs. From the laboratory have come other contributions. The basal metabolic rate is elevated. The blood iodine is increased. Another characteristic may now be added: an increased loss of iodine in the urine (Curtis and Phillips).

CONCLUSIONS

Biochemical progress has thus opened a new approach to the iodine relationships of thyroid disease. The thyroid gland is a principal storehouse for iodine and doubtless exerts a regulating effect upon iodine metabolism. However there is evidence to indicate that iodine has another function in nutrition separate from that of forming two-thirds of the thyroid hormone.

Consequent clinical investigation has established the significance of the blood iodine as a measure of thyroid function. It is an aid in the diagnosis of toxic goiter. The significance of the urinary loss of iodine is becoming clearer upon investigation and the increased excretion of iodine in the urine of patients with hyperthyroidism is of manifest consequence.

Diabetes mellitus is characterized by an increased blood sugar and a sugar diabetes. In the more recently recognized hyperparathyroidism, there is found an increased blood calcium and a calcium diabetes. Now we add that patients with hyperthyroidism present an increased blood iodine, and during certain phases of the disease an iodine diabetes. These findings throw light on several poorly understood features of toxic goiter.

By investigating iodine metabolism, it is becoming possible to leave the earlier empiricism and to adopt a more scientific use of iodine in the prevention and treatment of goiter. In this direction lies progress.

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Discussion

WALLACE I TERRY, San Francisco The painstaking studies of Dr Curtis and his associates are a distinct addition to our knowledge of the relationship of iodine to the thyroid gland Much of our use of iodine in goiter is empiric and haphazard and it is to be hoped that continued research by Dr Curtis will put its use on a scientific basis

The technique of the microchemical iodine determinations is beyond the province of the usual hospital clinical laboratory, but many medical schools have chemists who can carry out the method with sufficient exactness to give us data from the various goitrous and non-goitrous regions It would be most interesting to compare the readings for iodine in the thyroid gland, the blood, the urine, the feces, and the foods of Tibetans, for instance, with similar readings of people who live in distinctly non-goitrous regions Many of the Tibetans spend all their lives at altitudes of 18,000 feet or more where the soil is presumably washed free of iodine and where endemic goiter is exceedingly common, according to the reports of travelers Possibly the normal level of 12 gammas per cent of blood iodine is maintained, but it seems reasonable to expect that the elimination of iodine from the kidneys and intestines would be found below normal in these Tibetans

Toxic adenoma of the thyroid and hyperplasia, or exophthalmic goiter, have been considered by some to be essentially the same disease Against this theory are the following points one is slow in onset and development, the other is rapid, exophthalmos is not found in toxic adenomas unless there is also some hyperplasia of the thyroid proper, the basal metabolic rate may be subnormal, normal, or increased in toxic adenomas, whereas it is uniformly increased in exophthalmic goiter, the clinical courses of the two diseases are quite different. It seems to

me that Dr Curtis has added another point, namely that the blood iodine is higher in exophthalmic goiter than in toxic nodular goiter

The prevention of excessive regeneration after resection of the thyroid for hyperplasia by the administration of iodine succeeds well in some cases and fails in others Is the difference due alone to inadequate resection of the gland, or to insufficient doses of iodine or do patients react differently to iodine?

We know that the thyroid gland in exophthalmic goiter can utilize only a small fraction of the total amount of iodine contained in an ordinary dose of Lugol s solution given before operation. Why should we not give small doses and would there be any advantage in giving an organic form of iodine rather than the inorganic?

I feel that Dr Curtis and his associates are in a position ultimately to answer these and many other queries about iodine

THE DIAGNOSIS OF ENDOMETRIAL HYPERPLASIA[1]

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As much has been written regarding the research work on hyperplasia, I will not discuss the subject in great detail I should say, however, that were it not for the investigative work that has been carried out by the various workers abroad and in this country, the treatment of uterine bleeding from hyperplasia would have advanced but little. The details of these investigations have been discussed in Fluhmann's classic paper and in a recent paper by my colleagues (1) In these papers the notable contributions of the California investigators have been thoroughly discussed

The chief symptom of glandular cystic hyperplasia of the endometrium is bleeding In many cases this bleeding is indistinguishable from that produced by other conditions, and in order to arrive at a correct diagnosis, a diagnostic curettage with a study of the scrapings is necessary The experience of the past years has shown convincingly that much more diagnostic accuracy can be obtained from the ordinary history and physical examination than is generally regarded as possible Our experience has been that the newer methods of obtaining uterine biopsies are so satisfactory that diagnostic curettage can be eliminated in a large percentage of cases Studies of the material obtained from the uterus have been most interesting and instructive From them has originated a large number of investigations of fundamental importance, as well as of practical significance It is the purpose of this paper to discuss the diagnosis of the condition in the light of these studies

CLINICAL CONSIDERATIONS

The disease is more frequently encountered than is generally realized and is perhaps the most common form of hemorrhage that the gynecologist encounters It occurs at all ages but is most common after the thirty-fifth year Frequently there is a history of childbirth, abortion, or debilitating disease A noticeable number have had pelvic operations or ovarian resections Endocrine stigmas are frequently present, they are more common in the younger groups than in the older

Bleeding is the chief symptom It is often preceded by a definite period of amenorrhea It is painless, profuse, and usually prolonged The bleeding is checked from time to time, and then tends to recur On examination there may be found constitutional evidence of the cause or the effect of the disease Anemia is of course to be expected The basal metabolic rate is generally low, but rarely does it reach the frank myxedematous level The galactose tolerance test is variable, it may be normal or low Achylia gastrica is sometimes noted On pelvic examination the cervix is often found to be soft and may be open The uterus is variable and may be normal in size, or enlarged and thickened, frequently it contains fibroids In typical cases there is an ovarian enlargement resulting from the presence of a follicle cyst

DIFFERENTIAL DIAGNOSIS

Eighty-five per cent of the cases of uterine bleeding are due to one of the five following conditions cancer, abortion, fibroid tumor, extra-uterine pregnancy, or endocrine dysfunction I impress this on my students by making them remember the word "cafee," each letter in the word standing for one of the five etiological factors There are many local and constitutional conditions besides the five mentioned that may produce uterine bleeding, but they are limited to 15 per cent of cases Abortion is differentiated from hyperplasia by the history of pain, the examination of the fragments that are passed, and the use of the Aschheim-Zondek or Friedman test Extra-uterine pregnancy is sometimes mistaken for hyperplasia I was deceived by this in a private patient this last summer She was quite fat and had never had a regular monthly cycle She had been bleeding for 2 weeks before she applied for treatment There

[1]Presented before the Clinical Congress of the American College of Surgeons San Francisco, October 28–November 1, 1935

was nothing unusual found on physical examination. A vaginal examination disclosed the cervix a little soft the uterus normal in size and position and the appendages not palpable. The usual routine biopsy was taken from the endometrium and basal rate the next morning showed −10. A provisional diagnosis of hyperplasia was made. In a few days she had rather a severe pain that brought her to her knees and was associated with a fall in blood pressure. An examination at the hospital showed a very distinct mass and at operation an extra-uterine pregnancy was found. It is well to bear in mind that both hyperplasia and extra-uterine pregnancy have uterine bleeding and pelvic masses. If an accident has not occurred to the pregnancy both may have masses and be painless. In a condition like this, the Friedman test will be of great assistance. Fibroids sometimes offer a perplexing problem in differential diagnosis. Both cause uterine bleeding and an enlargement of the uterus. In a certain number of fibroids, the bleeding comes from the associated hyperplasia. Fibroids *per se* do not cause bleeding unless the tumor encroaches on the endometrium, or unless a fibroid polyp becomes ulcerated. The chocolate flow or spotting before or after the period is rare in fibroids. Unless it is definitely determined which is responsible for the bleeding, the patient may receive treatment for one and be suffering from the other Under certain conditions the treatment of the two is essentially different and if this point is borne in mind many proposed operations will prove unnecessary

The differential diagnosis between cancer of the body and hyperplasia is most important, and an error here may mean an unnecessary loss of a life. A close liaison between the laboratory and the clinician is absolutely essential I am firmly convinced that in teaching and also in large hospitals, the department of obstetrics and gynecology should maintain its own pathological laboratory headed by one who is an expert in this special form of pathology Cancer of the uterine body usually occurs in older patients than does hyperplasia. I have never seen the two conditions associated together in the same patient, nor have I ever seen hyperplasia as a forerunner to cancer Both conditions have uterine bleeding and both frequently have some enlargement of the uterus The diagnosis must depend on the biopsy Our department has found 7 cases of unsuspected cancer of the body of the uterus in the last year by means of the biopsy instrument. If this instrument is not at hand curettage must be used for biopsy purposes. It should also be carried out if the biopsy specimens obtained with the instrument are suspicious or unsatisfactory An accurate diagnosis must be made. Cancer of the body demands a radical operation. Hyperplasia may be treated by conservative measures. The prognosis of the disease as regards life is good although fatal cases have been reported. Some patients for no apparent reason, spontaneously recover while others continue to bleed and require treatment. Pregnancy may occur after a spontaneous recovery In other instances a cessation of the bleeding is followed by long periods of amenorrhea which are permanent in the older age groups.

In all cases in which the differential diagnosis is not clear an exploration of the uterus is advisable. This can be done by means of the curette or the biopsy instrument. The first instrument which we used was an ordinary hollow metal cannula (5) This was passed into the uterus, and strong suction was made at several points by means of an attached syringe. In the majority of cases satisfactory tissue was obtained. Lorincz has modified the method by the use of suction obtained from a motor driven pump Novak has recently recommended this modification. We are now using a small metal punch which can be passed through the cervix as easily as an ordinary uterine sound. A bite is taken from the endometrium, then the position of the instrument is changed and another bite taken. The instrument is then withdrawn and one is agreeably surprised to find two good sized pieces of tissue large enough to satisfy the most exacting pathologist The method has been used hundreds of times in our clinic It is not painless, but the pain is never severe enough to require an anesthetic It is used routinely as an office or dispensary procedure.

The instrument, of course, can be re-inserted an endless number of times and as much tissue as desired can be obtained Some have objected to the method on the grounds that it cannot completely explore the cavity of the uterus as well as the curette, and it must be admitted that this criticism is just It is our practice first to use the biopsy instrument, and, in doubtful cases, to supplement it with the curette We are unaware of any cancers that have been overlooked In one case in which a curettement was done, a non-malignant endometrium was found and the bleeding continued A subsequent biopsy revealed a cancer We routinely use the method in all suspected cancer cases, as we believe that the danger of disseminating the growth is less with this method than with the curette In case a cancer is not found, curettage might be indicated

The interpretation of endometrial tissue, as well as the treatment of endometrial lesions, requires an understanding of the physiology of the female sex cycle Before these two important phases of the subject are considered, it would seem wise to review the physiological essentials briefly

Following menstruation, the endometrium undergoes a gradual proliferation up to the time of ovulation which occurs at about the ninth postmenstrual day Then the epithelium ceases to proliferate and begins to undergo secretory changes When menstruation begins, the epithelium disintegrates and is cast off These cyclic changes in the endometrium are dependent on cyclic changes occurring in the ovary In the latter organ there is a period of follicular ripening following menstruation On or near the ninth postmenstrual day, this process terminates in the rupture of the follicle and the discharge of the ovum Following follicular rupture or ovulation the lining cells of the ruptured follicle begin to grow and to form a corpus luteum During the process of follicular ripening, the ovary secretes a hormone which stimulates the growth of the endometrium After ovulation the corpus luteum furnishes an additional hormone known as progestin The proliferative changes produced in the endometrium by estrin are modified by progestin in such a manner that the secretory or premenstrual endometrium results This premenstrual endometrium is cast off at the time of menstruation The actual cause of the menstrual bleeding is considered by some to be a special menstrual hormone originating in the anterior pituitary Others believe that menstruation is a degenerative process resulting from a decline in the ovarian hormones At present the preponderance of evidence supports this latter view The menstrual bleeding which follows the removal of the human ovary containing the corpus luteum lends support to this theory

The important studies of Smith and Engle and Zondek and Aschheim have conclusively demonstrated the dependence of the ovary on the anterior lobe of the hypophysis If the anterior hypophysis is removed the ovarian function ceases, this in turn causes a cessation of endometrial activity There is likewise a cessation of endometrial activity if the ovary is removed These facts indicate that the pituitary influence on the endometrium is mediated by the ovary It is known that the ovary, in turn, has a reciprocal action on the anterior pituitary The exact nature of this action, unfortunately, is not known at present

From a correlative study of ovarian and uterine changes, Schroeder found that the uterine changes before ovulation were caused by a hormone from the follicle, and those after ovulation by a hormone from the corpus luteum In endometrial hyperplasia he found no corpora lutea, and he concluded from this that the endometrial changes were the result of a failure of ovulation This resulted in a persistent follicle which stimulated the hyperplastic growth of the endometrium Experimental proof of Schroeder's contention of an abnormal follicular stimulation producing the hyperplastic changes has been advanced By injecting spayed rodents with estrogenic hormones, typical hyperplasia has been produced This work has recently been confirmed in monkeys (12) and in man (4)

The study of known cases of endometrial hyperplasia by means of biopsies taken every few days in the same patient has been most interesting and instructive Cases have been observed over a long period of time The

endometrium is not always constant, but varies from time to time. At times it is typically hyperplastic at other times it is similar to the normal interval endometrium. Bleeding may occur from the endometrium of the frankly hyperplastic type or from the one resembling the normal interval endometrium. In the latter instance a section would be considered as normal by the pathologist if judged by morphology alone. However if considered in the light of the menstrual history and with the knowledge that this type of endometrium is simply an early stage in the development of frank hyperplasia, the diagnosis becomes obvious. It is advisable therefore, to obtain biopsies near to the onset of bleeding and to consider the menstrual history as well as the section before arriving at the pathological diagnosis.

Endometrial hyperplasia is fundamentally a disorder of the hypophyseal ovarian relationship The nature of this disorder varies, and there are several possible variations. In addition, the hypophyseal ovarian relationship is influenced by other constitutional conditions such as tuberculosis, hypothyroidism, or protein starvation, etc. The bleeding is to be considered only as a local symptom of an underlying general condition. To stop the bleeding is to administer symptomatic treatment. To recognize the underlying condition and to correct it, which at once relieves the bleeding is to administer curative treatment. An attempt to recognize this underlying condition should be made in all cases by means of the recognized clinical methods which are used in this type of work and which are familiar to all studying the ductless glands. If such an attempt is not made the patient may be relieved of a symptom but may still retain the primary condition In a general way curative measures alone should be used in the younger patients. In older patients, curative and symptomatic measures may be indicated. Among the curative measures of value are anterior lobe substance, anterior pituitary gonadotropic hormones, dihydroxy estrin benzoate, thyroid extract, progestin, and the gonadotropic substances of pregnancy urine. Their objective is to restore the normal hypophyseal ovarian relationship. Among symptomatic measures, curettage is to be considered as a simple temporary hemostatic. It usually stops the bleeding, and is of use before curative treatment has had an opportunity to take effect. The use of snake venom has been highly recommended for its hemostatic qualities. Hysterectomy is rarely indicated and is reserved for those young women in whom curative measures have failed. Radiation depending on the dosage, may be either stimulative or depressive. Stimulative doses are indicated in ovarian underfunctions in young subjects, while depressive doses are used at the time of the menopause. In the menopausal group curettage followed by radium has proved satisfactory

The replacement of the curette by the biopsy instrument and the use of X ray therapy instead of radium has eliminated the necessity of hospitalization for many of these patients and to an increasing number has proved an easy and satisfactory solution of the problem.

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SOME ASPECTS OF MATERNAL NUTRITION[1]

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THERE has existed in Canada during the past 5 years the increasingly vexing problem of the inclusion in the family food budget of an adequate and well balanced allowance for the pregnant or nursing mother This is especially true if the family is on relief, or if the wage-earner's pittance demands the economy exercised by relief measures The mother then must be instructed in not only what kind and amount of food to eat and drink, but from what foods the essential elements are easily and cheaply obtained Moreover she must be shown how her food needs can be blended with the ordinary family meals so that a too great inconvenience in food preparation may be avoided.

The foregoing facts are generally known, it is true, but it is our opinion that there is lacking a definiteness in both the application and dissemination of that knowledge to obstetrical patients We propose first to offer a brief summary of the dietary needs of the pregnant and nursing mother, and then to show how these can be secured easily and with relative economy

It is best that no rigid diet be prescribed for the average pregnant or nursing mother, as obviously the individual need varies greatly The average gain in weight during the gestation period should be approximately 14 per cent of body weight, or 20 to 25 pounds, spaced 3 – 10 – 10 pounds during the trimesters (4, 7) Following delivery the weight falls to a level of 5 to 10 pounds above the starting point, at which level it should remain throughout the lactation period The basal metabolic rate during the first half of pregnancy remains approximately constant, but during the last 4 months it rises gradually until just prior to the onset of labor it is 20 to 23 per cent higher than at the onset of pregnancy, following delivery the rate falls relatively rapidly to the original level (8) The average woman of sedentary habits requires 2,000 to 2,500 calories per day during gestation, and 2,500 calories during lactation, obtained from carbohydrate, fat, and protein During the second half of pregnancy, the increased caloric requirement must be adequate to cover the needs of the growing fetus, and later during lactation to furnish milk Common sources of carbohydrates are bread, crackers, biscuits cake, pastry, cereals, macaroni, rice, tapioca, sugar, syrup, honey, jams, fruits, and vegetables Fat is used in the form of butter, cream, lard, crisco, drippings, and salad oil The appetite usually dictates the intake, which, however, must be supplemented by protective foods except when fruits and vegetables are eaten

The building foods are of protein and mineral origin A minimum protein intake of 70 to 100 grams per day obtained from animal and vegetable sources is necessary Animal protein obtained from meat, eggs, fish, fowl, cheese, and milk should constitute at least one-half the total protein intake Vegetable protein obtained from cereals, vegetables, and legumes supplement and act as animal protein savers, but as they are inadequate sources of amino-acids should not be used as the sole source of protein supply During pregnancy the maintenance of a positive nitrogen balance is important, in order to replace losses of the maternal tissues, to furnish adequate nitrogen for the growth of the fetus, and to build up a protein reserve for use during lactation The protein should be in assimilable form, should contain a selection of amino-acids to spare loss of body nitrogen, and should be accompanied by sufficient carbohydrate and fat to provide an adequate caloric requirement, which in itself will effect a protein saving This necessity is evident when we consider the relatively greater growth of breasts, uterus, placenta, and fetus itself, during the latter half of pregnancy, moreover, we should remember that, during lactation, the mother should furnish daily 7 to 15 grams of protein for the child alone A deficiency of protein

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may cause nutritional edema, poor muscular tone, lowered resistance to disease, and poor milk supply

In the pregnant and lactating state, a minimum of 18 milligrams of food iron per day is essential for furnishing the tissue with sufficient oxygen for metabolism. The best sources are liver kidney red meat, egg, dried or fresh fruits and vegetables, and molasses. This supply is necessary during gestation for maintenance of the maternal organism for the growth of the fetus, and for storage in the fetus to provide for the lack experienced during the early months, when milk is the sole food. A deficient maternal intake may provide sufficient reason for the secondary anemia so common during the latter half of pregnancy

Calcium lack provides the most glaring deficiency in northern Alberta. Its presence in a minimum quantity greater than 1.6 grams per day is necessary for fetal growth and protection of the maternal organism from disease. The logical source is milk, but an inadequacy can be supplemented by cheese egg yolk, dried fruits and vegetables. A deficiency may result in lowered resistance to disease, muscle pains especially in the legs, dental decay and maternal or fetal rickets.

The phosphorus requirement, 1 to 2 grams per day is insured by the ingestion of an average supply of animal protein. It is necessary for calcification of bone and nutrition of nervous tissue, and must occur in a definite ratio to calcium to insure normal bone deposition a deficiency naturally upsets this balance as do physical and psychic upsets, and previous states of nutrition

An adequate iodine ingestion is secured from water and vegetable foods in districts where it is in sufficient quantity in the soil We believe the inclusion of one sea food, fresh or canned each week provides the necessary supplement. In our province iodized salt is used, but the advisability of this where an adenomatous thyroid exists is questioned

Sufficient salt is contained in the average diet adequately to satisfy the daily need of 0 5 gram. That there is a distinct surfeit is shown by the average ingestion of 10 to 20 grams per day We have found that, during the later months of pregnancy a rapid increase in weight accompanied by edema can be counteracted or at least arrested by a reduction of salt and fluid intake.

The regulating foods are found in water cellulose and vitamins. An optimum water balance provides for an efficient circulating medium aids metabolism, and allows for excretion, without undue storage in the tissues. During the first and second trimesters, an average intake of 2 quarts per day is usually necessary During the final trimester and especially when edema occurs, a reduction to 1 quart at least, with some restriction of foods of a high water content, such as melons, tomatoes, and citrus fruits, is necessary

Cellulose ingestion (bulk) is necessary to insure normal bowel function, and to effect satiety without undue caloric intake It proves more efficacious in the majority of cases if it is non-irritating The best sources are fruits vegetables, and cooked whole cereals.

The very fact of pregnancy itself and the nutrition of the pregnant woman as a whole, are influenced by the amount of vitamin in the diet (9) Vitamin A is not synthesized by the body consequently it must be ingested. But while it is stored in the body in large quantities, yet with the extra demand unless the intake is constant, the supply is soon exhausted The best sources are green and pigmented vegetables, egg yolk milk, butter and cheese. An added supply diminishes the chance of a morbid puerperium by forming a first line of defense against infection while a lack of vitamin A may cause early in pregnancy resorption of the fetus, or later promote a greater incidence of premature or stillbirths

Vitamin B is best contained in the green leafy vegetables legumes, tomatoes, citrus fruits, nuts meat, egg yolk, and brewer's yeast In adequate amounts it stimulates the appetite and influences growth A deficiency causes an impairment in the neuromuscular control of the gastro-intestinal tract, a decrease in the propulsive speed, and dilatation, resulting in atonic constipation It may also cause a prolongation of vomiting of pregnancy and later be a factor causing poly-

neuritis (11) For these reasons an adequate supply insured from the onset of pregnancy will alleviate or in many cases prevent the development of these complications

Vitamin C is usually found in sufficient amounts in the average diet containing citrus fruits It is not stored in the body but is readily transferred to the mother's milk, where it assists in infant teeth and bone development In deficient amounts it may lead to abortion or else to the developing of a debilitated fetus

Vitamin D influences calcium and phosphorus metabolism Its distribution in foods is limited, it is found concentrated in egg yolk, fatty fish, fish oils, and to less extent in butter, cheese, and liver The commonest source is cod liver oil In optimum amounts it lessens the tendency to fetal rickets, it allows for a greater absorption of calcium from the gut, and hence a greater quantity in the blood stream A deficiency creates a negative calcium balance with decalcification of bone, and is no doubt a definite factor in the later maldevelopment of primary and permanent teeth

Vitamin E is widely distributed in foods, in green vegetables, whole cereals, egg yolk, muscle meat, and seeds At the present it does not seem to have much influence on the pregnancy itself, although its use is advocated as an effective agent in the prophylaxis of habitual abortion

McLester (10) declares the American people are acutely food conscious and will eat anything that they are told is healthful Julian Huxley states that, were he able to dictate the food habits of a nation for one generation, he could add one cubit to their stature and double their resistance to disease Nevertheless, it is established that the diet is deficient in the protective foods, chiefly minerals and vitamins (9) One-third of the average North American diet consists of food prepared from cereal sources, mainly flour, and in its milling excludes practically all vitamins Of the remainder, meat forms a large part, the roasts, steaks and chops so commonly eaten are not, in the animal, repositories of vitamins The organ store-houses, liver and kidney, are but rarely eaten Refining sugar eliminates both minerals and vitamins The delicate centers of vegetables so pleasing to the palate, obtained after removing the outer leaves, have, in the denudation, been robbed of about four-fifths of their vitamin content Pasteurizing milk destroys roughly one-third of the vitamin content

The necessity for adequate vitamin intake thus established should engender in our minds the need for carefully instructing pregnant patients as to their food requirements It should be almost unnecessary to state that a complete physical examination, including urinalysis and blood count, be performed on each patient, where possible, at her first examination, yet, such a procedure, we are sorry to say, is not the case routinely in general practice Too often, after the elicited fact of missed menstrual periods, a perfunctory abdominal or pelvic examination is performed and the patient is told she is pregnant (often by herself only too well realized), to be careful of her diet, and to return later In reply to her inquiry regarding food, she is told not to eat too much meat and to be careful, surely a very indefinite help to a woman whose every part is being definitely upset by this physiological process! Moreover, this may easily be remedied as the doctor is able now to obtain readily and cheaply various pamphlets printed by the federal and dominion governments on diet in pregnancy (5, 6, 12, 13) These yield the requisite information and these he can distribute to his patients if he does not wish to advise them himself

A simple outline of the protective foods around which the menu should be planned throughout pregnancy and lactation is based on a daily intake of

a 1 quart of milk, raw or cooked, supplemented twice each week by cheese

b 2 cups of vegetables, 1 fresh when possible

c. 1 cup of fruit, citrus fruits or canned tomatoes should be included three times a week

d 1 cup of cereal, whole cooked, supplemented for 2 or 3 days each month by uncooked grain germ

e 1 medium sized serving of meat, fish, fowl or eggs, with liver added once each week

This will furnish sufficient protein minerals and vitamins for resistance, well being and growth. Add the amount of bread, potatoes, macaroni, crackers, rice, cakes, sugar jelly jam syrup, cream, butter and salad oils dictated by the appetite, and regulated by the gain in weight to supply energy and make the diet attractive and satisfying Any variation over a period longer than 2 weeks must meet or substitute these amounts.

With this in mind we interrogate the patient as to her appetite, likes, dislikes, and mode of eating. In our zeal for adequacy we must not, however overlook the fact as Alvarez (3) points out that some persons are sensitive to certain foods, and that eating of them may result in any of a host of conditions, ranging from heartburn to convulsions. We must then briefly investigate this possibility and, if necessary attempt to modify in form or substitute these offending foods

If during the pregnant or nursing period the mother cannot take milk we advise milk products. A surprising number of women cannot or refuse to take a sufficient supply of milk or its products. In these cases we advise one of the various calcium preparations on the market This is usually supplemented by the concentrate of vitamin A or D or both. As mentioned before, we regard wheat germ (obtained from any grist mill) as a valuable source of vitamin B It becomes rancid quickly though and must be purchased in *small amounts frequently*

If the hemoglobin is 70 per cent or less of normal, we prescribe an iron preparation, *usually Blaud's pills*

During the first trimester certain points are to be emphasized, briefly summed as follows

1 *Repeated small meals throughout the* course of the day with the largest meal preferably before retiring the first a salted cracker or *arrowroot biscuit before rising*, which act should be performed slowly and circumspectly

2 Avoidance of *combining solid food and* more than a minimum of fluid this prevents that "full" feeling and moreover makes harder any vomiting which *might follow*

3 Avoidance of fried or greasy food and excessive fat

4 Taking easily assimilable foods, such as, clear candy honey sugar in beverages jello, junket, blanc mange, baked potato, rice, and crackers.

5 If necessary prescribing an additional amount of vitamin B as in pabulum whole wheat cereal, brewer s yeast, or wheat germ

During the second trimester with nausea overcome or past the ordinary diet suffices. At this time the appetite is usually increased and the temptation is to overeat, with its attendant flatulence or heartburn. Cutting down on the amount taken at one time and avoiding solids and excess fluids together usually alleviates or obviates these symptoms A half glass of milk taken 10 minutes before eating, or 2 to 3 drops of oil of peppermint in warm water after eating, also alleviates this distress. A gain of 8 to 10 pounds during this trimester is usually achieved and should not be regarded with alarm.

During the last trimester the diet may remain unchanged, or better a slight increase in protein during the last month may be encouraged to prepare for lactation. If the gain in weight is too rapid we have found a reduction in the amount of sugars and starches, such as jam, jelly honey candy bread potato cake, rich desserts and pastry will often alone suffice If that does not suffice or if there is accompanying edema or hypertension, we reduce also the salt and water intake Our practice in this respect is to advise a fluid intake per day limited to 40 ounces, and avoid using salt at table. If necessary the daily fluid intake may be limited *to 30 ounces*, and all salt in food preparation omitted The weight is carefully noted each week or oftener to check the result of this *reduction* This varies slightly with the program *outlined by the Committee on Maternal* Welfare (2)

Supervision of the diet during the post natal period is equally important, yet alas, universally neglected Fluid, calcium protein, and vitamin B intake should at least be maintained and usually increased The caloric requirement is approximately 10 per cent greater than during gestation to cover the energy loss in transforming food energy into milk. An adequate protein intake is most

important, as Adair has shown, in providing a bountiful milk supply Two quarts of water, 1 to 1½ quarts of milk, an additional serving of meat or its substitutes, wheat germ when possible, all taken daily prove ideal When, of course, weaning time occurs, these diet constituents are reduced to the previous normal, unless reduction or gain in weight is attempted, when appropriate shifts are made

The foregoing applies to the woman of average weight For the woman who is underweight a greater gain is allowed, and her daily ration is increased even to 4,000 calories if necessary The mineral and vitamin content remain constant The overweight woman is limited in starches and sugars, with increased mineral and vitamin ration, in order not to reduce, but to keep her weight constant, or at most, secure but a slight increase in weight These conditions are maintained during the lactation period

Outdoor patients are treated in a manner parallel to that of private patients The problem here is threefold to keep the diet within her budget, to explain to the patient in simple terms the purpose and procedure of the diet, and moreover, to supervise as far as possible her carrying out of the routine

To that end a member of the dietetic department of the hospital is in attendance at our prenatal and postnatal clinic To her are referred all new cases, all postnatal cases, and all others that need re-instruction in all or some modification of the diet With her, the dietitian reviews the budget and presents to her the appropriate routine based on a "relief" expenditure which, in Alberta, averages $1 80 to $3 00 weekly for man and wife The whole food question has frequently to be straightened out, as often a poor distribution is found to be in evidence If a greater allowance is deemed necessary it is recommended, and, we are glad to say, is always obtained from the authorities

If there is too great a gain in weight, if nausea, vomiting, or other early symptoms of toxemia are in evidence, or the milk is failing, the patients are referred to the dietitian for the proper dietary instruction, based, we repeat, on the financial status of the patient Working thus in close co-operation with the dietitian, we have secured a uniform and more adequate supply of milk, and to date have practically eliminated the severe toxemias, save only those fulminating cases which providence at times thrusts upon us

This relation of diet to pregnancy and lactation is known in greater part to obstetricians and general practitioners, and yet it is our belief that too little attention is paid to instructing the patient in detail We are interested not only in the general well-being of the mother, before, during and after delivery, but also in that of her child, a future parent If then a more careful attention to her diet will enable her to surmount more easily the minor afflictions of pregnancy, and, perhaps, avoid toxemia, will enable her to withstand better a hard and prolonged labor, will enable her better to recover easily and quickly from that labor, and withal, to provide an ample and nourishing supply of milk for her baby, why then that attention is more than justified

SUMMARY AND CONCLUSIONS

1 We consider the problem of the undernourished pregnant and nursing mother a vital one

2 We have briefly outlined the food needs, energy, protective and regulating, and have indicated the common sources, and the results occurring in optimum and deficient amounts of each

3 We have outlined our method of instructing these pregnant and nursing mothers, both in private practice, and, with the aid of the dietitian, in the out-patient service, where the problem of cost is a major one

4 We believe that more attention to this detail of obstetrical care will yield in return, fewer complications, healthier mothers, and healthier, better nourished babies

We are indebted to the authors of the references noted, and recommend them for your perusal.

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Discussion

Francis Scott Smyth, M.D., San Francisco. I presume, since I am interested primarily in the health of infants and children, that I am to discuss maternal nutrition as it affects the offspring. We have the slogan "Every child has the right to be well born" yet the factors involved are numerous, baffling, *and frequently beyond our control.* Maternal nutrition is one factor which does seem to lend itself to a program of study and control. There has been sufficient evidence to justify correlation of maternal health and certain pathological conditions in the newly born. *However,* we must allow for the possibility that the effect of faulty maternal nutrition may not be manifest in the offspring until after infancy. Hence, the correlation may not always be apparent.

It would seem obvious that the fetus is entirely parasitic and must depend on maternal metabolism for both food and the excretion of waste products. I do not believe that the literature has been crowded with scientific data on the metabolic needs during human gestation. There are only 10 accurate reports on calcium phosphorus metabolism in pregnancy and even fewer analyses of fetuses. Far better data on calcium phosphorus metabolism are available in the dairy industry. *I do not wish to* imply that we lack sufficient information to endorse Dr. Conn's program or that we should wait for further scientific reports before a social application *is attempted. I would merely point out that as a* field of investigation the metabolism of the gestation period has not been overworked.

But presuming the maternal diet to be sufficient, *it is still possible that* faulty digestion or elimination will prevent proper nutrition of both host (mother) and parasite (fetus). Recognizing the greater food requirement during gestation, the frequency of vomiting is *paradoxical. Hence, as Dr. Conn's* program shows, dietary supervision is not merely a question of quantitative intake but must involve *quality and distribution. This is provided for by* the schedule of small, frequent dry meals to combat vomiting in early pregnancy.

The unique rôle of the placenta deserves discussion. *Recognizing it as a barrier* between mother and fetus, its selective action is phenomenal since the fetal tissues have a far different requirement from those of the mother. Any failure of placental function cannot but affect the fetal nutrition even though the mother shows adequate nutrition. And the converse also is conceivable that, within certain limits, the fetus may thrive while the mother may show some degree of malnutrition. While we have accumulated data on the pathology of the placenta, there still is much to be learned with regard to its function. The work on the rôle of the placenta in erythroblastosis of the newly born and the recent work of McKhann on immune body and hormone concentration is very stimulating.

Turning next to some of the social problems, I have wondered if Dr. Conn has not encountered some difficulty with regard to follow-up or "policing" the job. For even in our well established "Baby Clinics" the program of which was pioneer in social nutrition, we have frequently seen lip service given to directions but obvious failure in execution. In dealing with adults, I confess an impatience if not despair with the slow process of education and find myself sympathetic with dictatorial power on matters of public health. I think it is safe to say that at present when food is doled out to depression dependents there are better results than when money is given and co-operation regarding dietary advice is optional. But even if temporary control of the diet may be obtained, it should be considered only as a demonstration and cannot

supplant the slow educational policy so necessary for permanent improvement

Dr Conn quotes McLester "The American people are acutely food conscious and will eat anything they are told is healthful" He does not comment further that the barrage of food-faddists and commercial interests tends to drown out the voice of the medical profession This is not, I believe, because of indifference on the part of the profession, but because it lacks accurate information and methods by which a sensible program may be worked out Programs such as Dr Conn has outlined should be welcomed The excellent work of the food clinic of the Boston Dispensary can be mentioned as a model by which education and method reach both lay and professional groups

I believe specific programs can be worked out on the basis of our present knowledge even though considerably more scientific data would be helpful I believe that the baby feeding clinics already demonstrate what may be done by a proper program, and that perhaps one favorable result from the depression has been the opportunity to demonstrate similar results for expectant mothers Finally, I believe that from the pediatrician's point of view, a closer co-operation with the obstetrician may result in improvement in infant nutrition and perhaps a further reduction in infant mortality

EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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FEBRUARY 15, 1936

THE 1935 CLINICAL CONGRESS

THE clinical executive, and scientific sessions and exhibits at the Clinical Congress in San Francisco and Oakland epitomized clearly the widespread interests and activities of the College and its various committees.

Heralded in the keynote address by the chairman of the Board of Regents on the first evening of the Congress as marking the rededication of the College to educational work among surgeons, hospitals, and the laity the 1935 Congress accomplished all that was expected of it. The heart of its founder and late director Dr Franklin H Martin, would have been warmed and his confidence in the assured future success of the College strengthened could he have heard the personal tributes paid to his memory and could he have followed the carefully planned constructive actions of the governing board. Again it was proved that the spirit of the College is, as it always has been a dynamic one, ever looking in advance to meet new conditions arising in the surgical world.

It was appropriate that the rededication of the College to its high purposes should have taken place on new ground. For the first time the Congress was held in the far West and the undisputed verdict has been that the surgeons of San Francisco and Oakland more than justified the selection of their cities as the seat of the 1935 Congress. Under the leadership of Dr Howard C. Naffziger they provided for the visiting surgeons such a series of operative and demonstrative clinics as fulfilled one of the main reasons for the foundation of the Congress—an opportunity for its participants for postgraduate education of the highest type. The entire medical fraternity of the Bay cities co-operated with the Committee on Arrangements to make this Congress a success.

The clinics covered all of the surgical specialties Surgery of the eye, ear nose, and throat was the subject of numerous clinics, and the practitioners of these branches held special scientific meetings throughout the Congress Perhaps they, more than any others, have utilized the motion picture as a suitable medium for the demonstration of their art.

At the executive sessions it was found necessary to adopt certain amendments to the by-laws of the College to meet new administrative conditions. Judiciary action also occupied the careful attention of the officers. The progress reported by the chairmen of the various scientific committees and of the Department of Hospital Activities is published elsewhere. Much attention was focused on the work of the Committee on Graduate Training for Surgery In the report of which further study of the introduction of graduate

training in appropriate hospitals and a restudy of the requirements for admission to Fellowship in the College were recommended At the impressive and colorful Convocation, Fellowship in the College was conferred on 571 candidates, and the incoming president further emphasized the advantages of graduate training

Numerous sessions devoted to the problems of hospital standardization were largely attended and the progress made in this department was evidenced by the granting of approval to 2,523 hospitals In spite of the economic stringency to which these hospitals have recently been subjected, it was pleasing to note that their main topics of discussion centered around possible new ways of furnishing better care to their patients The increasing interest of lay boards of trustees in this work was gratifyingly demonstrated Approval of 198 cancer clinics, 708 medical services in industry, and many commercial products for hospital use marked further progress

The large attendance at the evening scientific meetings and the meetings sponsored by the scientific committees on cancer, fractures, and industrial medicine and traumatic surgery was ample evidence that the subjects announced for presentation had been selected with a view to their practical importance to practical surgeons Guiding principles and specific details in diagnosis, management, and therapy were ably presented, and it was interesting to note the significant fact that a consideration of injuries occupied a relatively more important place than it has in the past when compared with the consideration of diseases

The participation of the College in the education of the laity on health subjects was recognized by the holding of a Community Health Meeting The presence of more than ten thousand people at this meeting demonstrated the avidity of the public for such information and their recognition of the College as an authentic source for it Numerous radio addresses, newspaper articles, and talks before social clubs and high schools extended the scope of this educational influence

A practically continuous program of surgical motion pictures was presented, and the frequent overcrowding of the large room in which it was held again emphasized the appeal to the surgeons of this visual method of education and furnished convincing proof of the desirability of employing this medium to a still greater extent

Mention should again be made of the fact that the cornerstone on which the success of the Congresses has been built has been the operative clinics The reputation of the San Francisco and Oakland surgeons attracted a large registration to this Congress, and the surgeons and hospitals provided a series of daily clinics that has evoked universal expressions of pleased satisfaction from the visiting members of the Congress California surgeons perhaps as never before have thus contributed to the progress of American surgery

Not a small part of the educational influence of the Congress was furnished by the technical exhibits which have come to assume an ever increasing scientific aspect from which the surgeons cannot but be benefited

While strictly scientific exhibits have never received great emphasis at the Clinical Congresses, a number of national organizations with interests in common with the College this year presented instructive demonstrations of their work

The strictly technical side of their practice has never occupied the attention of the master surgeons to the exclusion of their peculiarly intimate and influential position with refer-

ence to the personal lives of their patients their relations with their confrères and to the community and the nation These ethical and civic responsibilities of the surgeon formed the subjects of the addresses of the retiring president and of Dr Sproul in his Fellowship Address and the ideas and ideals presented by these gentlemen merit the careful study of all surgeons. They will serve to point the way to a still higher plane for the surgeon in his community life and better enable him to play a vital rôle in a vital, human relationship. These considerations cannot be too frequently restated if the ideals of the American College of Surgeons are to be translated into accomplished practice.

BOWMAN C. CROWELL.

HOSPITAL STANDARDIZATION

THE eighteenth annual Hospital Standardization Conference of the American College of Surgeons was held in San Francisco during the Clinical Congress, October 28 to November 1 1935 Speakers at each of the sessions and demonstrations enunciated the practical application of the fundamental principles of hospital standardization. Their viewpoints were especially interesting because they represented mature thought and an accumulation of facts based on some 34,000 individual surveys of hospitals A summary of the proceedings of the Hospital Standardization Conference will be published in the March 1936 *Bulletin of the College*

The twentieth century hospital is characterized today as an institution in which every man woman and child, regardless of race, color creed or social status is assured of the best care that medical science can offer to the sick and injured It is an institution in which the physician the surgeon and the specialist are enabled to carry on their professional work in an environment in which they can apply accurate and proved methods of diagnosis and treatment and in which each member of the medical staff is afforded every opportunity to advance his knowledge of medicine. The twentieth century hospital is a scientific, educational institution.

The term "hospital standardization" if interpreted literally might suggest adherence to a definite pattern or a tendency to make hospitals more or less similar in plan construction equipment organization, and function Hospital standardization might also be interpreted as an effort to standardize the professional and non-professional workers in the hospital But such was never the intention of the initiators of the plan. At no time did they contemplate that the individuality of a hospital should be sacrificed The officers and field workers of the College, in promoting hospital standardization, have encouraged distinctive service in hospitals through the application of flexible and adjustable guiding principles in the organization itself and in the service which is rendered to the sick and the injured They have encouraged group thinking group discussions, group action, and group review and analysis of end results. This has not detracted from the individuality of the hospital, for after two decades of hospital standardization one is impressed with the distinctive character of each institution which is on the approved list of the College

The survey of 3 565 institutions in the United States and Canada registered with the College at the beginning of the year 1935 reveals the following results

One thousand, six hundred and fourteen of 1 703 or 94 8 per cent of hospitals of 100 beds and over were approved, leaving 89 hospitals, or 5 2 per cent not yet meeting the requirement

Six hundred and eighty-nine of 1,047 or 65 8 per cent of hospitals of 50 to 99 beds were approved, leaving 358 hospitals, or 34 per cent not yet meeting the requirements.

Two hundred and twenty of 815, or 27 per cent of hospitals of 25 to 49 beds were approved, leaving 505 hospitals, or 73 per cent not yet meeting the minimum requirements

In summary, 2,523 of 3,565, or 70 8 per cent of all hospitals of 25 beds and over were approved, leaving 1,042 hospitals, or 29 2 per cent not yet meeting the minimum requirements

It must be a satisfaction to every Fellow of the College to know that in 1918, when hospital standardization was inaugurated, 89 hospitals in the United States and Canada met the minimum requirements, but in the 1935 survey 2,523 institutions were accorded a place on the approved list

It is an accepted fact that in the majority of hospitals the active or attending staff is carefully selected and each man is competent in his respective field Generally, the professional work of this group is well controlled and supervised, and this results in better medical records, more frequent consultations, a larger volume of laboratory work, and a more thorough review and analysis of the clinical work If the medical staff is not properly organized, inevitably there is inadequate control To obviate such a situation the individual members of the medical staff and the heads of departments must be carefully selected, and the chief of staff must be a leader who has some knowledge of medical administrative affairs The medical staff organization may be "open" or "closed," but it is important in either case that the staff shall be supervised and controlled by its own personnel The advance of scientific, professional efficiency of the hospital is assured if the chief of staff and the heads of the clinical departments recognize and assume their responsibility

The weakest link in medical staff organization today is that very large, loosely organized, and generally uncontrolled group—the so called courtesy staff It is imperative that the administration of the hospital, through its medical staff organization, shall bring this group under better control, even though it may mean curtailment of revenue Every Fellow of the College and every member of the active medical staff should assume his share of responsibility for the work of the courtesy staff

One of the inherent though intangible benefits of hospital standardization is its educational value to the members of the medical staff When a physician is graduated from college he has a great mass of technical knowledge This knowledge must never become static, it must be broadened, adjusted, or even displaced This may be accomplished through clinical experience in a hospital, through the preparation of comprehensive medical records of patients, through the proper use of the adjunct facilities, and particularly through the clinical pathological conferences in which a doctor works in close association with his colleagues in an atmosphere of continuous, reciprocal postgraduate education Two decades ago when hospital standardization took root in America, less than 500 staff conferences were being held annually for the systematic review and analysis of the clinical work In 1935 more than 40,000 staff conferences were held, with an aggregate attendance of 800,000

The advancement of medical science depends largely on the accuracy of medical records Every progressive hospital today recognizes the value and necessity of medical records, filed in an accessible manner, readily available for restudy, reference, or scientific research Every physician, surgeon, and specialist privileged to work in a hospital should consider it his individual responsibility to provide a complete medical record of every patient who is entrusted to his care—a medical record which contains sufficient data to justify the diagnosis and to warrant the treatment and end-results The need for a "medical records consciousness" is apparent in every

institution, but this consciousness cannot be successfully acquired until the medical records are used extensively All too frequently the medical record room is a "cemetery where the records of patients are permitted to rest, undisturbed in peace. Continuous individual and group study of medical records is essential to the advancement of scientific knowledge.

Through hospital standardization increasing attention has been directed to adjunct facilities, particularly to the clinical and X ray laboratories. The greatest advance in these services in recent years has come through the advent of the approved pathologist and radiologist and the registered technician. Because of the limited number of qualified pathologists and radiologists, hospitals have been encouraged to share the services of major specialists in these fields. There are other adjunct diagnostic and therapeutic departments which are of value to scientific medicine, but each must be under a qualified medical specialist in the respective field if the services are to be properly administered

The problem of the division of fees is one of the earliest and most difficult with which the American College of Surgeons has had to deal. Since the inception of hospital standardization the College has whole heartedly and vigorously fought this practice in which the monetary rather than the merit aspect is the prevailing influence—the buying and selling of patients on a commission basis. Owing to the difficulty of obtaining tangible evidence it is impossible in every instance to take effective steps to combat the division of fees, but even well sustained rumors have been considered sufficient grounds for lowering the rating of a hospital or withholding approval. The College has exposed this practice through every possible means, and the blatant vicious types of fee splitting have either disappeared from communities or have been driven to cover but it is admitted that the practice still exists. A hospital is not conforming to the minimum standard if it knowingly harbors fee splitters, or even those about whom rumors of fee splitting persist. The College must continue its efforts to abolish fee splitting and in this as in every activity of the College each Fellow has a direct responsibility If the Fellows of the College themselves would assume leadership in their respective communities and educate the public as well as the medical profession at large the desired result could be readily attained. In a small rural community where fee splitting was the general practice a campaign was launched by the four Fellows of the College, first in the medical profession itself and later through a campaign which was carried to the public. Soon the practice was abolished, and today there are three accredited hospitals which serve the public in that community

Is it possible for every hospital which exists today to become standardized or to meet the minimum requirements? According to the latest hospital directory of the American Medical Association there are 6,634 registered hospitals in the United States, of which 2,361 meet the minimum standard. Some of the hospitals which are not on the approved list of the American College of Surgeons will not meet the minimum requirements because of lack of interest or because of an unfortunate background. It is to be regretted that a hospital can come into being today in almost any community merely by expressing good intentions and giving reasonable assurance of the observance of the laws of sanitation and of freedom from physical hazards Unqualified hospitals will be eliminated only when every hospital is required to meet minimum standards of construction equipment, organization and personnel before a license is granted. After years of study and preparation volun-

tary organizations have laid down minimum standards, now it is the responsibility of the governing bodies to see that these standards are enforced if the best interests of health and human welfare are to be served

Hospital standardization requires the whole hearted co-operation and support of every Fellow of the College It would be a noteworthy achievement if the College could establish its ideals and objectives in every institution which cares for the sick and injured in the United States and Canada There are many notable examples where Fellows of the College in their respective communities have been responsible for promoting hospital standardization in a distinctive manner, and it is hoped that every Fellow will lend his aid in furthering the hospital program of the College

Approved hospitals have had a large part in elevating the standard of surgery, which is the announced object of the American College of Surgeons But the facilities of approved hospitals have not yet been utilized to the fullest extent in training the younger surgeons This is a subject to which the College is giving special attention at this time, looking toward the establishment of three to five year residencies in general surgery and the specialties in many of the major hospitals

MALCOLM T MACEACHERN

PRESIDENTIAL MEETING, CONVOCATION

THE CONSCIENCE OF THE SURGEON[1]

ROBERT B GREENOUGH, M D F.A.C S Boston Massachusetts

In accordance with a wise provision of the by laws of the American College of Surgeons, the president-elect serves a *novitiate of one year* During this period it is his duty to make himself familiar with the details of organization and administration of the College before he is inducted into office and becomes in fact the president of the College with the duties which are definitely prescribed for that office. At the end of his year of *experience as president, it is again his duty and* his privilege to bring to the attention of the Fellows such suggestions and recommendations as appear to him important for the further advancement of the College. In fulfillment of that duty I stand before you tonight to discuss briefly a matter to which one of my predecessors referred a *few years ago as one of the "intangibles" of surgery*—the conscience of the surgeon.

With the extraordinary advances in surgery which have taken place in the past twenty years, it has been made possible for us to increase enormously the efficiency of our service to mankind These additions to our material resources, however have tended I think to divert attention somewhat from the more spiritual and moral aspects of the practice of surgery which have been *in the past* and must always be in the future, the guiding principles of our service to humanity if we are to continue to retain the respect and the devoted appreciation of the community which has been accorded us in the past

Conscience is defined as moral sense or "a sense of right and wrong To this may be added *conformity to one's own sense of right in conduct or to that of the community*" There has thus become attached to the concept of conscience the idea not only of ability to discern the right, but to act accordingly and with this has come a sense of responsibility to others and to the community as a whole Possession of a conscience becomes thus one of the finest attributes of human character and distinguishes the higher civilizations from that of man in the primeval state

The science and art of medicine is of necessity so little understood by the laity that they are obliged to entrust their lives and their welfare to the physician rather upon faith in his character *and reputation than upon actual experience of his* abilities. Thus, conscience becomes one of the most important elements in the character of the physician Especially is this true as regards the surgeon, for his activities are carried on largely in the seclusion of the operating room and often only his colleagues and his assistants are in a position to judge intelligently whether his ministrations to the sick and injured are as efficient as the existing state of surgical knowledge and resources will permit. It is this fact that seems to justify a review of some of the features of the practice of surgery which require a keen conscience on the part of the surgeon and a definite sense of responsibility to his patient, to his hospital, to his colleagues, and to the whole community

We must start with the definite understanding that physicians and surgeons are not born as supermen they merely have to become so They are influenced by the same considerations of ambition selfishness, greed, and jealousy as afflict other human beings. As children we are obliged to learn by our training by the example and counsel of our elders and instructors, and by the standards of ethics and morals of the community in which we dwell, as well as by our innate sense of justice to resist these impulses with more or less success, and to determine our conduct accordingly that we may play the part which is allotted to us in modern civilization. Such training brings to the medical schools a group of young men not greatly different from others who have prepared themselves to study for law business, architecture or other professional careers. *From the beginning* of the medical school course however and especially in the last two years when the student comes more in contact with clinical work in hospitals, he begins to appreciate the peculiar relation of personal responsibility to his patient which the physician must be ready to accept as the first and foremost condition in the practice of his profession

In school and hospital, the medical student's work is carried out under *supervision. He is able*

[1] Address the Retiring President recorded before the Annual Congress of the American College of Surgeons San Francisco October 1, 1937

to observe the responsibility which his surgical instructor assumes when he entrusts an operation, a dressing or any surgical procedure to the neophyte. He realizes how closely his work is observed and criticized or commended, and how every precaution is taken to ensure that difficult operations and procedures demanding considerable surgical skill and judgment, shall not be entrusted to the beginner until actual experience has demonstrated his qualifications for the appointed task. This is the period in the student's training when his surgical conscience begins to be developed, and it is of vital importance to the success of its development that this sense of responsibility to the patient should be demonstrated and respected by the individual members of the hospital staff under whom he obtains his training. A low standard of ethics on the part of a hospital staff is inevitably reflected in the lowering of the moral sense of graduating interns and in a short time readily debases the ethical standards of the practice of medicine and surgery in the whole community.

On completion of his internship service, or if he takes the larger period of training as a resident, which is coming to be recognized today as a necessary qualification for specialization in surgery, at the end of his resident service, the young surgeon qualifies by passing the state or national board of registration and obtains a license to practice medicine. This is today an all inclusive license and permits the physician to practice medicine, surgery, obstetrics, and indeed any of the specialties for which he may consider himself qualified. Here again his conscience is his only guide. We seldom encounter today, however, instances of willful disregard by the surgeon of the dictates of conscience in attempting to undertake operative procedures for which he is in no way qualified. This fact is due in no small degree to the educational and disciplinary measures instituted by the American College of Surgeons and to the doctrine of staff responsibility which has been so vigorously promoted by the department of hospital standardization.

The apprentice system of education is ideal in its application to the career of the junior surgeon, provided always that the surgeon with whom the apprentice works is ethically, as well as surgically, qualified to give the desired training. The association between the competent, conscientious surgeon and his junior assistants may be one of the most delightful and stimulating of human relationships. Unfortunately, not all surgeons are sufficiently altruistic to be able to withstand jealousy of the highly competent assistant or associate who is beginning to stand on his own feet, nor are all assistants and associates sufficiently loyal to their preceptors to avoid the suggestion of competition as they approach the inevitable end of their apprenticeship. There is in this case the need of a keen conscience and an innate sense of justice and fair play on the part of the surgeon, as well as of the assistant or associate.

In relation to his patients, perhaps the most vexing problem to the surgeon is provided by the judicial consideration of the indications for or against operation. The patient is often referred to the surgeon by one of his medical consultants with a diagnosis made and advice to submit to operation given. Shall the surgeon permit himself to be made the mechanical assistant of the attending physician? Not at all! The full responsibility passes at once to the surgeon when he accepts the patient. He must convince himself that the circumstances warrant the operation, that all reasonable methods to confirm the diagnosis have been made, that there are not sufficiently important contra indications to prevent the operation, and that it is in the best interest of the patient that the operation be performed. Here again the surgeon must consider himself in the light of a trustee of his patient in surgical matters and act accordingly. The reputation of being easily influenced to operate, is one which no surgeon can afford to sustain, and his conscience alone should serve to protect him from this accusation.

Surgical internes and residents in the hospital receive their training in the whole field of general surgery, and this indeed, is as it should be. As his experience develops, however, he finds that one or more of the special fields of surgery appeal especially to him, and he devotes himself to carrying his knowledge of these special subjects to a higher degree of development than in other fields. To this end he may attach himself temporarily, at least, to one or more of the special clinics and services which have been developed of late years in many of our larger hospitals. His general surgical work must not be sacrificed, but a certain amount of special knowledge is an asset of enormous value to the young surgeon who is starting in general surgical practice, and brings him opportunities for co-operation and assistance to older men that are of the greatest help in establishing him as a useful and respected member of the surgical community. He may in this way also readily lay the foundation for such original and investigative work as still happily remains the supreme ambition of the members of the medical profession, in the hope of making some worthy contribution to the advancement of medical science.

The American College of Surgeons seeks to indicate by admission to its Fellowship, that by training and by experience its Fellows are qualified to practice either general surgery or one of its designated special branches, and that the ethical standing of the surgeon and the reputation he holds among his colleagues is above reproach. The world advances, however and the surgery of today is very different from that of twenty years ago. The training and experience which was sufficient for qualification as a surgeon in 1912 must be considered inadequate today. It would be a sad commentary on the wisdom of the founders of the College if its by-laws were not so worded as to permit the qualifications for Fellowship to advance with the progress of surgical science. Fortunately this is the case, and it is and has been the duty of the College, through its credentials committees, to raise the standards of admission to Fellowship in the College as the years go by.

Surgery is taught in our medical schools as one of the two great departments of medical science. Every graduate in general practice is expected to know the essentials of surgery and in an emergency, where more experienced surgical aid is not available is expected to do the best he can for the patient. Such circumstances justify attempts to perform surgical operations by the general practitioner which would not be tolerated under other circumstances where better qualified surgical experience was accessible. Here the conscience of the physician plays a most important rôle. He must place his services at the disposal of the patient, and he must use such judgment and such skill as he may have to meet the emergency until more expert service can be procured. In doing this, he must be guided by conservatism and must have the interests of the patient so at heart that he unavoidably is forced to view the problem with unbiased appraisal of his own abilities a proceeding in which his conscience alone can guide him to a correct decision. The same situation arises when the surgeon, trained and qualified in general surgery is faced with an operation or a method of treatment which requires special experience or equipment not available in his community. If the situation is an imperative emergency, he must do the best he can with what he has. If not, his conscience will make him see the advantage to the patient of obtaining more expert aid by sending the patient elsewhere, or bringing in some more qualified consultant.

The subject of surgical fees is again a question in which the conscience of the surgeon must play an important part. It is a well established axiom that maximum fees for surgical service can be paid only by the very well-to-do, and that the greater part of the surgeon's work must be performed either gratuitously as is customary in free hospitals and clinics and too frequently also in private practice, or at fees far below the maximum amount accepted in the particular community as reasonable and proper remuneration for the service rendered. Many medical societies have attempted to establish fee tables for medical and surgical services, but the spread between maximum and minimum fees is usually so great as to make its application to the individual case extremely difficult. It is undoubtedly true, also, that the standards for medical and surgical fees in one community differ greatly from those in another and hard and fast lines can rarely be drawn without consideration of the local standards.

In general there is a disposition on the part of the public to consider the surgical laborer worthy of his hire. It is usually only when the patient is for some reason dissatisfied with the service given, or when he comes to the conclusion that the fee charged is exorbitant, that complaint is made. These difficulties can be avoided to a great extent, if financial considerations are discussed beforehand, but there seems to be an almost unaccountable reluctance to adopt this plan. The surgeon hesitates to introduce this subject lest he be thought mercenary in his motives, and too often patients fail to make inquiry about expenses, in the assumption that the operation must be done in any case and, at the moment, the matter of expense is to them of least importance. Since there is always of necessity some discussion, as to hospital accommodations, however the subject of expense of surgical services can readily be brought into consideration. From this point of view it is the patient's financial welfare rather than that of the surgeon which is under discussion and mention of surgical fees beforehand is not likely to be misconstrued. If this practice were more often followed complaints of overcharging would be greatly diminished. In this connection, also, it should be emphasized that it is by no means always the largest fees which lead to criticism but rather those which, while justifiable to the average patient, represent to the individual of moderate means, a sum out of all reasonable proportion to his resources. A system of medical practice under which people may be forced to mortgage their property and to expend for necessary medical or surgical service a great part of the resources which they have accumulated in years past to safeguard their dependents as well as their own declining years, can be fairly criticized. Free or

partial payment hospital service, adequate, if not luxurious, is available today in all of the larger communities and in many smaller and less thickly settled districts in this country for those who deserve such treatment The medical profession has always been, and will continue to be, ready to give its service gratuitously, if necessary, or at reduced fees to those in need To avoid injustice, however, plain talk is necessary and false pride, either on the part of the surgeon or of the patient, must be avoided Luxuries should be eliminated Consideration of the essentials is the first necessity The conscientious surgeon will make this clear to his prospective patient This applies not only to the straightforward discussion of the patient's resources and of his financial obligations and responsibilities as well, but it involves also the necessity for the surgeon to consider that he is acting as the trustee of the patient in advising him to obtain such type of hospital accommodation as is suited to his means The desire of family and friends to mitigate as far as possible the dangers and discomforts of surgical hospitalization leads many to assume expenses which are quite unnecessary, for hospital accommodations, for special nurses, for the services of special consultants and, indeed, for many special and expensive laboratory methods of diagnosis, which, while occasionally necessary, are often quite superfluous in routine cases The conscientious surgeon will seek to protect his patient from unnecessary extravagance along these lines, just as surely as he endeavors to protect him from the dangers of anesthesia and of sepsis in the operating room

In his relations with other physicians and with other surgeons, the surgeon's conscience must be keenly alive to the necessity of avoiding injustice to others, as indeed he desires to escape injustice to himself The "Golden Rule" is still an adequate guide to conduct for the surgeon as for other individuals in the world today, although there are those who maintain that of late years, under the stress of competition and depression, its observance is not as popular as it used to be

The physician in general practice selects one surgeon rather than another to whom to send his patient, primarily because he has confidence in the chosen surgeon's ability and integrity It is unthinkable that such considerations should be thrown in the discard, and the selection of the surgeon made because of financial considerations offered by the surgeon in the form of splitting fees Such buying and selling of patients requiring operation in the past, has been a grave reproach not only to the surgeons and physicians who so debase their profession, but to the communities in which these grave abuses of professional honor have existed The campaign which the American College of Surgeons has carried on to eliminate this pernicious practice is one of its greatest achievements, but is is undoubtedly true that in certain localities fee splitting still exists, and the College cannot rest until the evil is eradicated for good and all

In his relations with his consultants the surgeon must so conduct himself as to protect the interests of the physician as well as of the patient. Here lies a divided responsibility, and circumstances may make it impossible that both interests be adequately protected It is the patient's welfare, however, which must be paramount, and that of the physician must give way if the two are definitely in conflict.

If the physician is seriously at fault this fact must be acknowledged, but explanation of such extenuating circumstances as are present should be given due consideration, and every effort should be made to protect the physician from unjust and undeserved criticism Many suits for malpractice owe their origin to hasty and often unjustified criticism of a physician by other physicians who are often ignorant of the actual facts and who base their conclusions on insufficient or incorrect evidence supplied by the patient or his sympathetic friends

The relation of the surgeon to his colleagues and surgical competitors gives ample room for the conscience to determine right and wrong behavior It is true, of course, that there is intense competition for surgical practice, not only in smaller communities but in larger cities as well The preparation and presentation of papers at medical meetings is recognized as the only legitimate form of "advertising" of medical or surgical proficiency, although hospital appointments, teaching positions, and medical society office and committee work, all undoubtedly serve the purpose of making the surgeon better known among his colleagues It is true that even this legitimate advertising may be overdone The surgeon who is prolific in medical literature, especially if his communications are not impressive, acquires a reputation which in the long run defeats his purpose by exposing him to some good natured ridicule from his colleagues and competitors Beyond this point, however, the medical code of ethics does not permit the surgeon to advertise his accomplishments, and especially must he avoid any direct approach to prospective patients by newspaper or other publicity which features his individual professional accomplishments The medical code of ethics, which forbids such practices, is

looked upon by many of the laity as an antiquated and unnecessary custom, but they fail too often to appreciate that it is devised, not for the protection of the physician, but in the interests of the public.

Without this code, the public would be exposed to the same exploitation by unscrupulous physicians, as that to which they are now subjected by advertisements and high pressure radio publicity methods of quacks, cultists, and the manufacturers of patent medicines and commercial remedies. The physician who is competent and proud of his profession avoids even the semblance of advertising and is vigorous in the enforcement of the code of ethics to which we all subscribe. This code in no way prevents a patient from changing from one physician to another if dissatisfied and in no way prevents the physician from accepting a patient who has been in another physician's care. The only necessity is that this be done openly and aboveboard and that a definite understanding of the change and of the occasion for it be had by both physicians. The character and temperament of the physician or surgeon is so significant a part in the patient's choice of one or another medical attendant, that no reflection upon the physician's professional competency is necessarily involved in such a change and often the physician who is relieved of responsibility in a given case is quite as pleased as is the patient when such a change is properly brought about.

The most disagreeable duty which falls upon the surgeon is that which results from his responsibility to the community and to the medical profession as a whole to take his part in the protection of the public from incompetent or unworthy members of his own profession. In such cases, whether it be in a court of law or by participation in a trial board, the surgeon's duty to his colleague must give way before his duty to the community and to the profession as a whole. Here again his conscience must determine his action, while his professional judgment must be as impartial as he can make it.

I have dwelt upon some of the more difficult problems which beset the surgeon in the ethical practice of his profession, but there are countless more which occur to trouble him from day to day. The pledge to which we all subscribe when we are admitted to Fellowship in the American College of Surgeons, covers in broad terms many of the matters I have set before you tonight. It is well that we should ever bear in mind the terms of this pledge which we have taken since they are helpful in the determination of our conduct from day to day. Let us remember always that, however great our knowledge or our technical skill, it is the application of that knowledge and skill to the service of the community that is required before it becomes of value. It is the character of the surgeon and his moral sense of responsibility, in other words his conscience, which finally determines the effectiveness of his service to the community and the respect which he himself and the science and art of surgery to which he devotes his life, is accorded by the public.

THE AMERICAN COLLEGE OF SURGEONS AN EDUCATIONAL INSTITUTION[1]

A Tribute to Franklin H. Martin

GEORGE CRILE, M D, F.A C S, Cleveland, Ohio

ORIGIN AND UNDERLYING PRINCIPLES

If one were to ask the American College of Surgeons whether it would not be well for it to enter into educational activities, such a question would be as naive as it would be to suggest to Harvard University that in view of its buildings, equipment, and personnel, it would be well for the University to become an educational institution

In the unparalleled development of undergraduate instruction during the years prior to the founding of the American College of Surgeons, the undergraduate faculties in America had neither the time, the staff, nor the facilities to take over postgraduate instruction on a large scale Forty years ago the ambitious surgeon was confronted by a dilemma either he must go on as best he could, "on his own," or else he must go abroad, where better postgraduate opportunities could be secured

For many years prior to the founding of the American College of Surgeons, there had been an insistent demand, particularly by members of the special surgical societies, that some organization be founded whose prime function would be the elevation of the standard of surgery in the United States and Canada This demand had come in particular as a result of the organization in 1903 by a small group of surgeons of the Society of Clinical Surgery, which, as its title suggests, recognized the difference between teaching of the theory of surgery and training for the practice of surgery The programs of the meetings of the Society of Clinical Surgery in America consisted of operative and dry clinics and of laboratory demonstrations In keeping surgeons abreast with surgical progress, it was at once obvious that the value of the demonstration of the practice of surgery far exceeded the presentation of the theory of surgery in papers

This new pattern of mutual teaching evoked such enthusiasm among the members of this society that similar groups were organized in various fields of medicine and surgery and in the specialties, and Franklin H Martin envisaged the possibility that this principle could be made available on a large scale to surgeons everywhere

Using his journal, Surgery, Gynecology and Obstetrics, as a means for organizing and publicizing such a movement, he founded in 1910 the Clinical Congress of Surgeons of North America, the first meeting of which was held in Chicago, November 7 to 19, 1910

The program of the Chicago Congress consisted of clinics and demonstrations supplemented by evening addresses upon the surgical problems of the day That this educational principle met a universal need was attested by the facts that this first Congress was attended by 1,300 surgeons, that at the end of the first week of the Congress an invitation was received from the medical profession in Philadelphia to hold the second Congress in that city, and that before the conclusion of the Philadelphia Congress in 1911, many delegations were urging that New York have the Congress in 1912

For some time previous to the inauguration of the Clinical Congress, the need of an American College of Surgeons had been seen and discussed, and the insistent demand for such a permanent organization came to a focus at the Clinical Congress in New York in 1912 It was largely through the personal leadership of Franklin H Martin that a committee was formed to formulate a plan of organization, and that on November 25, 1912, a charter was granted by the State of Illinois for the establishment of the American College of Surgeons The American College of Surgeons was patterned after our federal government and the government of the Dominion of Canada, as it recognized states and provinces as units in the organization

A board of regents, a board of governors, a credentials committee for each state and province, and a Central Credentials Committee were established, and Dr Franklin H Martin was appointed director general The committee which drafted the original by-laws, rules, and regulations consisted of the following Franklin H Martin of Chicago, Edward Martin of Philadelphia, Emmet Rixford of San Francisco, John B Murphy of Chicago, Rudolph Matas of New Orleans, Albert J Ochsner of Chicago, Charles H Mayo of Rochester, Frederic J Cotton of Boston, George Emerson Brewer of New York, John M T Finney of Baltimore, Walter W Chipman of Montreal, and George Crile of Cleveland.

[1] Annual Oration on Surgery presented at the Presidential Meeting of the Clinical Congress of the American College of Surgeons San Francisco October 28–November 1 1935

The original roster of Fellows that is, the Founders of the College, included 546 surgeons of Canada and the United States

The first president of the College was John M. T Finney of Baltimore, and succeeding him in the earlier years we find such names as William J and Charles H. Mayo, George E. Armstrong, John B Deaver Harvey Cushing, Albert J Ochsner Rudolph Matas, and Walter W Chipman.

Such names as these give testimony of careful organization, of representation from various parts of Canada and the United States, and of various types of surgery Throughout these years the leaders in undergraduate education and the leaders in the practice of surgery—men experienced in organization—have made up the governing groups —the Board of Regents, the Board of Governors, and the various committees. Each has left his impression, and the result is seen in the present, not static, but continually evolving pattern of the College.

To achieve the purposes of the College, land, buildings, and endowments had to be provided. Realizing this, many of the Founders and of the subsequent Fellows of the College became life members of the College by the payment of $500 each, the amount thus contributed constituting a substantial part of our capital fund.

Although the educational activities of the American College of Surgeons started at once after its organization for 7 years it had no home of its own In 1920, through the leadership of Franklin Martin, in association with a group of Fellows of the College and of citizens of Chicago, the handsome headquarters and valuable land at the corner of Erie street and Wabash avenue was acquired, and later the beautiful Murphy Memorial building and library was presented to the College by the family and friends of the late John B Murphy In 1928 a plot of ground was purchased by the College at the corner of Rush and Erie Streets as a site for the future Hall of the Art and Science of Surgery These properties have an approximate value of $1,250,000

ADMISSION REQUIREMENTS

Every educational institution has certain requirements for admission, and the status of the institution in the educational world depends largely upon its adherence to those requirements. To this end the American College of Surgeons has established a credentials committee in each state and province which is made up of Fellows of the College who are elected by vote of all the Fellows from the respective state or province These credentials committees have set up standards for admission to the College and are the first to pass upon the qualifications of a candidate for fellowship These standards are based upon the actual fitness of the candidates by training, character and experience as these qualities have been evidenced in their daily work and in their daily contact with Fellows of the College in the hospitals in which their work is being done. These committeemen are themselves leaders and know best how to judge the qualifications of the men who are practicing surgery in their respective territories. Each state and provincial credentials committee holds one meeting a year when the applications for fellowship of the respective state or province are considered.

The strength of the American College of Surgeons lies largely in the fine, impersonal judgment of the local credentials committees which constitute a group of more than 900 leading surgeons throughout Canada and the United States who are serving this important purpose. In this unheralded group is vested the primary responsibility for the numbers and quality of the Fellows of the College.

In addition to the recommendation by the state and provincial credentials committees a "written examination" is required in the form of a report of 100 histories of major operations—50 histories of operations of the candidate's own cases and 50 of operations at which he has assisted or for which he was the responsible surgeon. These histories must be submitted to the committee on history reviews, which is comprised of members of the surgical divisions of faculties of medicine. Its members meet weekly during several months of each year. They have served without pay for years and over a million case histories have been reviewed by this committee of the College

The standards set by credentials committees and by the committee on *history reviews* have been steadily raised, increasing emphasis being laid upon the length and adequacy of the candidate's training, as the College encourages long term training in surgery

The recommendations of the state or provincial credentials committees and the findings of the committee on history reviews are then considered by the central credentials committee whose recommendations are finally acted upon by the Board of Regents, individually and collectively Upon this Board rests the final responsibility for determining the candidate's eligibility for fellowship.

It is apparent that this method of selecting the candidates by the leaders in the profession in the states and provinces, in which they live and practice, provides a safer and more accurate criterion from the educational point of view than the results of an examination of textbook knowledge which would give little evidence of the fitness of the candidate to assume the high responsibilities of the practice of surgery

It does not seem to be a question of how many the College should admit to fellowship but rather of how many are ethically and professionally qualified for fellowship If the College is to carry out its purpose it should aim to admit to fellowship every surgeon who is ethically and professionally qualified and who is recognized as a safe and efficient surgeon in his community This will stimulate others to attain the standard set by the College and is the most effective way to raise the standard of surgical competency

In other words, the American College of Surgeons is not a restricted society for those who have achieved a position of exceptional merit, that office is filled by a number of special societies, membership in which is eagerly sought and is conferred only as a special recognition of merit. The membership of the American College of Surgeons, on the other hand, is composed of surgeons who have proved that they are safe surgeons from the standpoint of the patient and who wish to participate in a program for the elevation of standards of surgical and hospital practice

One sometimes hears the criticism that there are men in the College who do not merit membership for one or another reason This same statement may be made of every organization that exists, of every church, and of every club In our organization we believe that this does not detract from the innate merits of the fundamental principles of the organization On the other hand, we have all the barriers that can reasonably be set up to prevent the ingress of the undesirable candidate, and the judiciary committees in each province and state are constantly having cases referred to them for investigation of rumors regarding individual Fellows

The executive committee refers the findings of the judiciary committees to the Board of Regents for final action From time to time Fellows are expelled from the College for conduct which is injurious to the good order, peace, or interest of the College, or derogatory to its dignity, or inconsistent with its purposes, and though these cases are not publicized, the names of such individuals are no longer included in the roll of Fellows

HOSPITAL STANDARDIZATION

The very first educational problem that presented itself was that of hospital standardization This involved an educational program for the vast network of hospitals in the United States and Canada The number of hospitals which have now reached or exceeded the minimum standard is 2,523 The value of their land, buildings, and endowments is approximately $3,500,000,000 The number of surgical operations performed annually in the hospitals of Canada and the United States is approximately 2,500,000

Hospital standardization is distinctly an educational program It has affected not only the members of the hospital staffs but the general public as well The public by this effort to promote better hospitalization has come to look upon the hospitals as the most important agents in the promotion of health and the advancement of human welfare

The hospital information and service department of the College is a part of this great educational enterprise as through this channel hospitals may secure authoritative and complete information concerning problems of planning and construction, organization, administration, management, and standardization

The hospital standardization program which has extended over 18 years has involved over 34,000 surveys, including more than 3,600 hospitals The major rôle in this colossal task has been played by the associate director, Dr Malcolm T MacEachern In all of this work the College has been aided by the great medical and hospital organizations, including in particular the Catholic Hospital Association, originally under the leadership of the Rev Charles B Moulinier

DEPARTMENT OF CLINICAL RESEARCH

To further its educational program, the College of Surgeons has organized departments in the form of committees to each of which a specific field of activity is assigned The work of these committees is correlated and promoted by the associate director, Dr Bowman C Crowell

Thus there is the Committee on the Treatment of Malignant Diseases organized by our retiring president, Dr Robert B Greenough, who was succeeded by Dr Charles A Dukes, the present chairman The prime purpose of this committee is to make the benefits of contemporary knowledge of cancer available to every surgeon Under its auspices 250 cancer clinics have been surveyed among which 198 have been approved The College has information concerning 116 other cancer clinics which are in some stage of formation

There is the Registry of Bone Sarcoma, originally established and presented by Dr E A Codman which investigates and publishes criteria for establishing the diagnosis of malignant bone tumors. The Registry now contains approximately 1,900 complete case records and an increasing number of 5 year cures is being reported annually The nomenclature has been made uniform and the procedure for accuracy in diagnosis and effectiveness of treatment has been widely disseminated. Dr Dallas B Phemister is the present chairman of the Registry

There is a Committee on Fractures which first under the successful chairmanship of Dr Charles L. Scudder and now under Dr Frederic W Bancroft, has established a standard for minimum equipment for fracture treatment in hospitals. Its constant effort is to stimulate interest in and to improve the treatment of fractures. The committee has established better means of caring for the treatment of fractures in hospitals and has promoted a national program in first aid and transportation of the injured.

There is a Committee on Industrial Medicine and Traumatic Surgery of which Dr Frederic A Besley is chairman. This committee reports an increasing interest in this department of the educational program of the College on the part of leading industries. A minimum standard for medical services in industry has been established and 1,314 industries have been surveyed of which 712 have been approved The great importance of these two committees—on fractures and on industrial surgery—is emphasized by the fact that last year in the United States there were 16,000 deaths from industrial accidents and 36,000 deaths from motor vehicle accidents The total disabling injuries in the United States in 1934 amounted to 9,911,000

There is the recently established Medical Service Committee of which Dr Robert B Greenough is chairman, the purpose of which is to formulate general principles on medical economics for the ethical guidance of Fellows of the College

The work of the Committee on Medical Motion Pictures, under the chairmanship of Dr J Bentley Squier, has been of important educational value. This committee reviews medical motion pictures, thereby stimulating the production of such films along proper ethical and technical lines. Medical motion pictures can be a valuable adjunct in the teaching and dissemination of medical knowledge. To this end the committee has outlined an extensive program covering the production of important films pertaining to fundamental sciences, medicine, surgery and various specialties, hospitals, nursing and the promotion of health. Through special committees on the review of films, the College has examined many hundreds of films each year approving those which are of high educational value for medical students and physicians. Through this means the value of the motion picture from the educational standpoint is fully realized.

A Committee on Graduate Training for Surgery under the chairmanship of Dr Samuel C. Harvey has recently been organized The need for such a committee might be questioned since all activities of the College are concerned with educational problems. This committee, however, has been appointed to study graduate training for surgery Years ago the long-time training of interns in surgery was adopted at Johns Hopkins Hospital, but this offered a special opportunity to a limited number of men This principle however has been extended to other hospitals. It is now expected that a larger number of hospitals will enter into this plan by which more men expecting to enter the field of surgery and the surgical specialties may have longer and more efficient training

Through the Library and Department of Literary Research, instituted in 1921 the College is able to stimulate educational research among clinicians everywhere The extensive library with its thoroughly trained staff makes it possible for the College to comply with requests for information on all medical and surgical subjects by providing abstracts, bibliographies, reports of researches, and package libraries in all languages from available literature. Through proper organization of the accumulation of valuable material, the service can be offered at less than actual cost Already thousands of clinicians the world over have received valuable educational assistance from the Library and Department of Literary Research of the American College of Surgeons.

As in every College the work of these departments consists in securing all available knowledge in their respective fields and of imparting that knowledge to the students, that is, the Fellows. The specific purpose of the College of Surgeons, therefore, is to assemble knowledge pertaining to surgical education—the art and science of surgery hospitals, and other activities having to do with the health of humanity—and to disseminate this knowledge through the Fellows of the College who work on this great educational campus.

Important as are the activities of the American College of Surgeons which are carried on in Chicago through the various departments of the College, they represent but a part of its educa-

tional activities The sectional meetings and the annual Clinical Congress, together with the hospital standardization program and the programs of the various College committees, make its activities international in scope Thus we may truly say that when a surgeon is admitted to fellowship in the American College of Surgeons and pays his life membership fee of $500, or his annual membership dues of $25, he matriculates in an educational institution which undertakes to give him the greatest possible facilities for his further advancement in the science and art of surgery Every hospital staff meeting, every committee meeting of the College, every regional meeting, every Convocation of the College, every set of histories submitted, constitute a part of the mass effort which is being made in behalf of the Fellows of the College In other words, the headquarters of the College in Chicago, together with all of the hospitals in Canada and the United States which have conformed to the minimum standard, constitute the campus of the American College of Surgeons It should be emphasized, however, that as in any academic college the benefits derived by each individual depend entirely upon himself

And now the American College of Surgeons is considering the establishment of another and most important department—the Hall of the Art and Science of Surgery The exhibits in this Hall of the Art and Science of Surgery will present not a static but a constantly progressing panorama of contemporaneous methods of surgery and of the applications in surgery of the allied sciences upon which surgery depends This department will be under the direction of Dr Crowell

TRAINING FOR SURGERY

The type of educational work that the American College of Surgeons has been fostering on a large scale is postgraduate education The undergraduate school is primarily concerned with the theory of surgery the American College of Surgeons is primarily concerned with the practice of surgery The training of a surgeon cannot be effected within a stated period of time with a final examination An examination in the theory of surgery alone could be no safe guide for judging the fitness of candidates for the practice of surgery An examination in the theory of surgery would not indicate whether the candidate has a surgical mind, thinks clearly, is skillful, and has good judgment and common sense, and whether he has ethical and moral standards

It would be as logical to weigh a man to see if he is honest as to examine him in theory to ascertain his skill and ethical standards The certificate of the undergraduate teacher should attest whether or not the candidate has enough theory and it may be said that the greatest surgeons living today probably could not pass an examination in the theory of surgery Leonardo da Vinci would not be judged by his knowledge of the theory of color, nor Beethoven by his knowledge of the science of sound

Students are taught the theory of surgery, they are trained for the practice of surgery The undergraduate teacher certifies to the theoretic qualifications of the student The American College of Surgeons certifies to the practical qualifications of the candidates for fellowship and matriculates them into the College as Fellows to train them in surgery during life Therefore it cannot be overemphasized that every one of us must be in college for the period of our lives, and that our advancement and our training should be as active in one period as in another All that the university can do in its examinations, all that the Credentials Committees of the College can do in regard to its requirements, is to candle the egg Undergraduate education and training for surgery have made enormous strides in this generation and now mass education for the men in practice is undergoing an equally striking development

There are two types of personalities in regard to whose work the teacher is apt to miss judgment One type includes the men with well developed memory mechanisms who easily acquire honors while in the university but who by the time they get their degrees and their postgraduate training lose the stimulus of their training and never have an independent growth These minds have been educated beyond their intelligence

The other group includes the men who annoy their teachers on account of their independent way of thinking and their independent point of view They often are not promoted and leave their hospital service early Their teachers, however, at some later time are surprised to find that among the more outstanding pupils are those who have been rejected but who have become the pillars of the temple Thus there are four periods through which the surgeon passes in his complete course The premedical course in which his progress depends upon character and training, the medical course in which progress depends upon character and training, the period of interneship in which progress depends upon character and training, and the later course in which progress depends upon character and continued training In this later course an additional and imperative incentive is added by competition with his fellows

It should be borne in mind that we are building not in the interest of the profession but primarily in the interest of the people at large. The automobile, the airplane and other methods of transportation—the machinery of civilized man—is so distributed on the farms and ranches and in the mines, on the highways, on railways and in the air, that everybody is on the front line so that in the case of an accident, a disease, or a surgical operation it is as necessary to have a good surgeon in the most remote place as it is to have one in San Francisco Los Angeles, Boston, New York, or Philadelphia.

Therefore our task is to see to it that there are good surgeons all over Canada and the United States, and wherever there is a human being who requires the service of a surgeon we must have a good surgeon and a good hospital.

No good surgeon can be made such by proclamation, and no pronouncement can prevent the trained, industrious student from becoming a good surgeon. Education and morals and ethics are matters of training This was well illustrated in our experience with the Eighteenth Amendment.

Thus the American College of Surgeons while not a postgraduate school in the ordinary sense of the word is a great educational organization whose fellowships are offered to all surgeons who have given sufficient proof of their surgical ability and ethical standards and who are ready to participate in the program of the American College of Surgeons for the elevation of the standards of surgical practice and of hospitals.

THE CREATIVE PERIOD OF THE COLLEGE

The 23 years which have passed since the foundation of the College may be considered its first or creative period This period closes with the College as the largest and most active surgical organization in the world. It is a self-supporting College It is free from debt. It has expended $3 727,099 in educational programs and has assets in land buildings and endowment of more than two million dollars. It is a College, not in name only but in fact. It presents the largest, most comprehensive postgraduate medical program offered by any educational institution. Under its own budget it has carried on its comprehensive program of hospital standardization under the leadership of Dr MacEachern until at the present time the hospitals of the United States and Canada and of other countries beyond the confines of this continent have benefited from its educational program. Its constructive campaign which has increased in efficiency through the years has brought to millions of patients untold benefits—better diagnostic laboratories, better clinical records, better pathological service better operating room facilities and, of especial significance, a finer spirit of co-operation among the staff members,—as evidenced by the fact that monthly staff assemblies in approved hospitals numbered 4,000 in the single year of 1934, with an aggregate attendance of over 800,000. It has established an educational standard, emphasis being laid on operative and diagnostic clinics follow-up studies and end-results clinical pathology case reports motion pictures, scientific exhibits, and group responsibility of the staff for the care of patients.

The College has held 23 annual Clinical Congresses and 175 sectional meetings. In this period the total attendance at the annual meetings and the regional meetings has amounted to approximately 121 500. The College has made contacts with the lay public in the presentation of the aims and objects of scientific medicine to approximately 400,000 people who were in actual attendance at community health meetings, to say nothing of the millions who have been reached through the press, the radio, and the 750,000 high school pupils who have been addressed by representatives of the College.

The American College of Surgeons thus brings to a close its creative period with its romance of high adventure, of trial and error of praise and blame, with net results as stated.

DR. FRANKLIN H. MARTIN

Dr Franklin H. Martin gave every atom of his strength and organizing genius to the American College of Surgeons during its creative period. He made the College and the Journal the passion of his life His name will ever represent this period now closing

Standing by his side, sharing the anxieties and perplexities of the problem, advising and aiding, has always been Mrs Martin. Her unheralded rôle of itself possesses enough significance to merit acclaim. Mrs. Martin received from Dr Martin and inherited the Journal SURGERY GYNECOLOGY AND OBSTETRICS. She is the sole owner of this great magazine For many years it had been the desire of Dr Martin that upon the death of himself and Mrs Martin this Journal should become the property of the American College of Surgeons Mrs. Martin fully agreed with this generous intention. Through her action this has now been assured The Journal SURGERY GYNECOLOGY AND OBSTETRICS, with its assets has been trusteed, the income to go to Mrs Martin during her lifetime and upon her death it is to become the property of the College

So at the end of its creative period we find the American College of Surgeons enriched by the gift from the citizens and medical profession of Chicago of its handsome home at the corner of Wabash avenue and Erie street, by the gift from the family and friends of the brilliant John B Murphy of the Murphy Memorial hall and library, and now to land and buildings is added the gift of the greatest surgical journal in the world—SURGERY, GYNECOLOGY AND OBSTETRICS

It is for me a great honor as the official representative of the 12,000 Fellows of North and South America, Europe, Africa, Australasia, and the Orient to proclaim the qualities, and to acknowledge our everlasting obligation to our departed leader, to express to Mrs Martin our deep appreciation not only of the gift of the Journal but of the even greater gift from Dr Martin and herself of prophetic vision, great achievement, and faithful friendship

THE TREND OF SURGERY[1]

DONALD C. BALFOUR, M.D., F.A.C.S., ROCHESTER, MINNESOTA

THE medical historian of the future probably will refer to the past fifty years as marking an era of unprecedented advance in all branches of medicine, and will hazard the prediction that it is doubtful if equal progress ever again will be made in the same period of time. Certainly in the field of surgery such a prediction seems well founded. In this era the great accomplishments of surgery have been made because anesthesia and asepsis made possible the application of knowledge of pathology, physiology, biochemistry and roentgenology and in turn a deliberate, scientific, and safe approach to every part of the body. Much of the extraordinary development in the knowledge of disease can be attributed to the fact that surgery provided a method by which the "pathology of the living" could be completely revealed and its effects studied. In the beginning of this era surgical exploration all too frequently revealed a condition which was obviously the terminal stage of a lesion that might have been satisfactorily dealt with in its incipiency. Surgery therefore, can be credited with giving the impetus to clinical and laboratory methods of identifying lesions in the early stages of their evolution. In some fields, surgery made possible recognition of the conditions under which lesions may occur. Thus, surgeons of all countries have added to knowledge of disease in its various stages and the ready availability of reports of observations made the world over has placed the present era in surgery in so distinguished a position.

Innumerable examples could be cited to illustrate the progress of surgery during this period. Major surgical procedures are now carried out with such safety that the predictions of surgeons only a few years ago are forgotten. The great surgeon Langenbeck, when Billroth was endeavoring to find a safe method of resecting the stomach for cancer, stated that he looked on the attempt as "only a quicker way of taking out of the world a patient whom it is impossible to save." Yet today this operation is routinely performed, with a resulting definite percentage of cures in cases of malignant disease and with consequent restoration of health to those who have benign lesions. Again, it is a far cry from the times of John Hunter who said, "To perform an operation is to mutilate a patient we cannot cure; it should therefore be considered as an acknowledgment of the imperfection of our art." The most significant trend of surgery has been the attempt to control, ameliorate, abort, and prevent those conditions which are known, or suspected, to be dependent on disturbed physiological processes. In the treatment of peptic ulcer, for example, the attempt to achieve by surgical measures the ideal in management of the disease—to effect permanent inhibition of a hyperactive function, particularly of the secretory mechanism—has resulted in the employment of a number of procedures to bring about such control in the simplest and most physiological way. The surgery of the sympathetic nervous system is an entirely new approach to the treatment of those diseases which are characterized chiefly by vasomotor spasm, and the future developments in this field of surgery probably will be as startling as those that have already been made. Again, the attempt to employ a similar method of approach in treatment of those conditions which may be dependent on normal or abnormal activity of the ductless glands may open up great possibilities for the surgical treatment of a wide variety of conditions which may be attributable primarily to altered physiological function, particularly of the vasomotor system.

The factors contributing to these great advances in surgery have come from every field of medicine. As already has been pointed out, surgery, in revealing the actual disease, gave the initial impetus to a more exact knowledge of disease. But second only to surgery have been the roentgen rays. The place of roentgenology in the diagnosis of lesions in every region of the body cannot be overestimated. Not only have these rays made possible detection of lesions before any method known at present can detect them, but, with biopsy and knowledge of cellular differentiation, accuracy in prognosis has been immeasurably improved. The fact that by roentgen rays lesions can be identified before clinical manifestations are present, has been an enormous benefit to mankind in making possible early and effective treatment. The recognition of pulmonary tuberculosis, of cancer of the gastro-intestinal tract, and of lesions of the skeletal system are examples to substantiate this fact. From the clinical and experimental laboratories have come those innumerable exact tests and observations which, when employed intelligently along with careful study of the

[1] Presidential Address presented before the Clinical Congress of the American College of Surgeons, San Francisco, October 14-18, 1935.

patient and the subjective and objective signs of disease, have added so much to diagnosis, prognosis, and successful therapeusis These factors in surgical progress, therefore, have been applied in strengthening the base on which successful treatment may be founded, namely, an accurate diagnosis It is certainly true that modern medicine has brought diagnosis more nearly to an exact science than ever before

The medical profession of America has played a prominent rôle in initiating and participating in the advances which have brought surgery to such a high level Haggard, in his address as retiring president last year, not only emphasized this fact but drew attention to the many important contributions from pioneer surgeons living in communities remote from medical centers, and to the superior opportunities which such environments afford Again, in North America the development of those collateral fields of medicine which have made modern surgery what it is today, has been conspicuous This development has come about chiefly through specialization Whether or not medicine has become too highly specialized, it always will be true, as Herbert Spencer pointed out, that it is only through specialization that progress can take place Specialization in establishing standards always will be necessary to determine the possibilities in any field of medicine, and for this reason specialization always will be the forerunner of improved methods of practice The influence of those engaged in special surgical fields is seen throughout America. In the smaller hospitals, which have been such an important feature in the development of medicine on this continent, the character of the work, whether the hospitals are staffed by specialists or not, gives unmistakable evidence of familiarity with the best diagnostic and therapeutic measures, knowledge of which has been acquired through travel, intensive graduate courses, and study of the medical literature The improvement of medical practice in the smaller communities has been such that the care of the sick in America is not excelled in any other country of the world

The situation which confronts the recent graduate in medicine who desires to become a surgeon is a perplexing one, for even a superficial knowledge of the extent of the field of surgery will, or shall, make him uncertain as to how much of this field he can master Whatever his choice may be, there is more and more evidence that he realizes the necessity for prolonged training to equip himself sufficiently for practice in either general surgery or in any special branch of surgery While it is true that because of natural aptitude and continuous and conscientious study many surgeons in America have become outstanding without a graduate apprenticeship, yet the great advances which have been made in recent years in all branches of medicine have rendered it more and more difficult for anyone to acquire real competence without an adequate training, so the quality of medical service in any community is in direct ratio to the training of the professional personnel

Just as the need for special training affects the young surgeon, so also does it bear on the whole practice of surgery The future of surgery in America depends primarily on the adequate training of those aspiring to a career in the field To demand, however, a protracted training while the opportunities for it are so unorganized as at present is not consistent, as recently has been inferred in an editorial in the *Journal of the American Medical Association*

"Growing demands for training in special fields of medicine have given greater significance to the available types of graduate instruction To present, as clearly as possible, a picture of existing opportunities for advanced study, the Council on Medical Education and Hospitals has obtained reports from all universities having faculties of medicine Two universities have separately organized graduate schools of medicine Twenty-nine report that they offer systematic courses of instruction for physicians An apprenticeship type of training through residencies or fellowships is available in fifty-three institutions Extension teaching of a less formal sort is conducted by nineteen schools, and as many more do not engage in any form of postgraduate work. Graduate teaching is a heavy tax on the resources of an institution, and not many of our schools are equipped to engage extensively in this work. This is particularly true of the intensive courses demanded by physicians who have already engaged in practice Generally speaking, they are able to pay in cash for what they want, but because of greater earning power and social responsibilities, they cannot devote any unnecessary time to this phase of training Younger men who have never practiced may be willing to pay for experience with time and services after the traditional manner of apprentices"

The evident need should be the incentive to make available sufficient opportunities for a fitting training in surgery

From what has been said, it is evident that the proper classification of undergraduate and graduate teaching in surgery is the first essential Undergraduate teaching in surgery should be restricted

to the teaching of fundamentals and general principles, while graduate teaching should carry out the training for practice in surgery through surgical residencies or fellowships. The granting of the right to practice surgery by state and national boards which require no practical evidence of competency, has been unfair both to the recipient of such a right and to the public. The American College of Surgeons was the first organization in the country to attempt to correct this evil by requiring evidence of experience and proficiency before implying it. The College indirectly has done much to keep before the attention of the profession the fact that an undergraduate course in medicine and a year's internship do not and cannot give sufficient opportunities for training in surgery to warrant certification of competency in surgery in these days.

The question therefore of the training which shall be required of the surgeon becomes of immediate interest and of particular importance in America, since in respect to requirements we cannot claim to be as advanced as are some other countries. The advantages which may grow out of our freedom from long established customs in surgery may be outweighed by the evils which may follow such freedom. That the medical profession is well aware of our shortcomings in this respect is seen in the establishment of qualifying boards for many of the surgical specialties. The methods adopted and practiced by the qualifying boards already formed have so much to commend them, that it is probable that in all fields of medicine similar boards will be set up to designate those qualified to announce themselves as specialists in the various fields. The effectiveness of such qualifying boards is dependent on the approval, support, and recognition of organized medicine and it is gratifying that such co-operation is being given.

The distribution of population in America creates another problem for investigation, namely it should be determined in what way the education of surgeons can be adapted to the varying needs of small and large communities. A graduate training in surgery of three, four or five years after completion of an internship is, to a large extent, not applicable in the small community and it seems imperative that some distinction be made in the requirements that various communities may present. The Council on Medical Education and Hospitals of the American Medical Association and the American College of Surgeons, in respect to establishing minimal standards for medical schools and hospitals, have already done much to solve this problem in proving that the hospital which cannot, or does not, acquire these minimal standards and does not select its surgical staff on the basis of competency and character sooner or later loses some of its standing in the community. With a better distribution of well equipped hospitals, the adequately trained young surgeon will find greater opportunities for applying his knowledge and ability. The surgical residencies which are available to the young graduate today seem to be sufficient, at least in number, to serve the need of those who settle in the relatively small community with the responsibility of dealing with those emergent surgical conditions in which the life of the patient depends on recognition of the emergency, a knowledge of what should be done, and the ability to do it. In the most recent study of the Council on Medical Education and Hospitals of the American Medical Association, there are listed 442 surgical residencies in the hospitals of the United States, and of these 73 per cent are for a period of a year. A twelve months surgical residency following an adequate internship should at least determine whether the resident possesses superior qualifications to justify continuing in a more extensive training, or whether the knowledge he has acquired could be applied best in the smaller communities. The investigations of medical schools, internships, and hospitals, which have so improved medical education and practice in this country could well be extended to include a study of the training which existing residencies offer.

The trend of surgery in America can be viewed with optimism. In every surgical field treatment is becoming more efficient and the willingness to discard apparently well established, major surgical procedures for simpler methods has resulted in some of the most remarkable advances of modern therapeutics. The irradiation of benign and malignant tumors and other lesions has completely altered the management of some of the most serious conditions, and there seems little doubt but that the applicability and the effectiveness of irradiation will steadily increase. The injection of sclerosing substances in treatment of varicose conditions, and the development of transurethral surgery are notable examples of a trend of modern surgery particularly obvious in America, namely the search for methods which will reduce morbidity and mortality to a minimum. Such advances have come from intensive effort expended by those highly skilled and widely experienced. It is in the co-ordination of these special fields and in the evaluation of various therapeutic measures that the American College of Surgeons has one of its most important functions.

In working out the problems touched on here, the American College of Surgeons should play an important part The purposes of the College are the highest, for its every activity is designed to elevate surgery and to improve constantly the quality of surgical service made available to the people of America In the fulfillment of these purposes a great debt of gratitude is due to the founders of the College, and to the vision, courage, and extraordinary organizing ability of its late Director General, Franklin H Martin It is not generally appreciated that the formation of a College of Surgeons in America twenty years ago could be undertaken only on the principles laid down by its founders The chief of these principles concerned Fellowship in the College To meet existing conditions, the requirements set up were characteristically American, the qualifications for Fellowship were based on proficiency and character, attested by those familiar with the candidate and his work The added provision that a minimal period of eight years must elapse after graduation from medical school before applying for Fellowship, largely eliminated the defects of any system which would grant Fellowship on the basis of scholastic standing only, for the most profound knowledge of basic sciences and of the theory of surgery does not necessarily make a competent surgeon Again, the College has given support and encouragement to its Fellows by the standardization of hospitals, by providing opportunities for attending clinics in medical centers, and by taking its part in the program of public education on which organized medicine has embarked The accomplishments of the American College of Surgeons are recorded in the status attained by American surgery today, and it is to be hoped that, in any modifications of the policies of the College, the ideals on which it was founded will always be retained

SYMPOSIUM ON CANCER

TREATMENT OF MELANOMA[1]

Report of Four Hundred Cases

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I HAVE great admiration for the committee of the American College of Surgeons that worked out the general scheme of this program. It is high time that some group seriously pondered over the problem and decided on what should be considered standard therapy in some of the major forms of cancer

Surgeons are apt to overemphasize the surgical approach to the cancer therapy Roentgen and radium therapists likewise overemphasize their form of therapy In general, those who employ both methods freely are convinced that irradiation in one form or another has gradually extended its field of usefulness while the surgical lines are a little narrower and more cleanly cut. However all now agree that definite types of cancer are preferably treated by surgery certain types by irradiation while other types are better treated by a combination of both surgery and irradiation. In another group, we do not yet know which is the preferred form of treatment.

My understanding is that the purpose of this symposium is to help crystallize the results of our experience in therapy and to attempt to arrive at a more definite conclusion on whether surgery irradiation, or a combination of these should be employed in definite types of cancer These conclusions must be based on a large experience and arrived at by judicial and careful studies of our cases

MELANOMA

The nomenclature of the malignant pigmented tumors has always been confused. Some dermatologists apply the name melanoma to certain benign heavily pigmented lesions and call the malignant tumors of this type malignant melanoma A generic term for the entire group is melanoblastoma which is subdivided into 2 classes—melanocarcinomas and melanosarcomas, depending on the preponderance of epithelioid or spindle cells in the tumors We employ the word melanoma to designate all malignant tumors derived from melanin-producing cells or cells capable of producing melanin, namely melanoblasts. The precursory lesions which may change to melanomas are called pigmented nevi.

Melanoma is one of the most malignant of all tumors. This tumor is important not only because of the attributes of extreme grades of malignancy but also because of the fact that no single tumor in the entire realm of oncology offers the clinician more divergent opinions as to what constitutes proper procedure.

In this paper I shall discuss only the more common and practical problems which the melanotic tumor present to the practitioner In the past 10 years many original and valuable studies have been made on the subject of melanoma, so that we today are more enlightened on its finer points in histopathology some of which have been made possible by silver staining We know more about the chromatophores more of its relationship to other tumors such as the neurogenic sarcoma more of the coincidence of intermedin output from the hypophysis more about its clinical behavior

Melanoma arises from a specific mesoblastic cell, the melanoblast and possibly also from epithelial cells which have been modified by the production of pigment. The melanoma may be primary in the skin, the choroid coat of the eye, the rectum, the vagina, the intestine, the meninges, the mucous membrane of the mouth and cheek, the sclera of the eye and the nail bed. The diagnosis is chiefly confused with that of pigmented epithelial papilloma and with the pigmented neurocnevus. In many instances arriving at the correct clinical diagnosis is simple, and in many instances, is almost impossible However, the jet black elevated, smooth, shiny melanoma cannot be easily mistaken for other lesions. It is the variants of this tumor that lead to confusion for example, the non-pigmented melanoma is difficult to distinguish from a benign nevus.

Melanoblasts are present in great abundance in two tissues, especially the skin and the eye. In

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the eye the pigmented cells of the retina as well as the pigmented mesoblastic cells of the choroid, have the function of melanin production In the skin, the heavily pigmented areas are more frequently the sites of melanotic tumors particularly in the region of the external orifices A site in which melanomas may occasionally occur and which is liable to be overlooked is the cleft between the toes The nail matrix and the conjunctiva occasionally contain melanotic tumors Primary tumors are infrequent in the viscera, the majority of reported cases when subjected to careful analysis, are evidently secondary or metastatic tumors of unknown primary origin

As a rule this lesion is congenital In our series most patients described it as an inherited lesion There were some instances, however, which seem authentic because of the intelligence of the patient, where there was no lesion until a short time before the development of the melanoma

The frequency of occurrence of nevi and melanomas is similar for the face, neck, back, and upper arm, but in other regions there is an interesting disparity. Melanomas are of frequent occurrence on the soles of the feet and on the genitalia, in which regions nevi are seldom observed Nevi are more frequent on the upper extremity than on the lower extremity, whereas melanomas are more frequent on the lower extremity than on the upper extremity These findings are in agreement with our observations that certain melanomas of the feet and genitals originate on skin which is apparently free of pigmented moles

In our cases 20 per cent of the melanomas were situated on the head and neck, 16 per cent on the feet, 18 7 per cent on the trunk, 8 7 per cent on the leg, 10 9 per cent in the eye, 6 5 per cent on the arm, 1 3 per cent on the skin of the breast, 1 per cent on the male genitals, 3 per cent on the female genitals, 1 3 per cent within the oral cavity, and 2 per cent were of undetermined origin

The frequency of pigmented moles is generally underestimated In a careful survey of over 300 people, Pack has found that the average person has at least 20 pigmented moles Last winter I heard the chairman of an important cancer committee state before a large lay audience that one should have every mole on the body removed It is obvious that he was not very familiar with the common problems which present themselves to the clinician As the average person has about 20 pigmented moles, if he has reached the age of 40, there must be some common sense rule developed to guide us Such a rule would be the following *Leave the brown moles alone, be concerned only with those which definitely contain black pigment*

In many instances melanoma, although present in a particular site, may lie dormant for many years However, under certain extraneous influences it is not unusual for the tumor to commence growth and dissemination These factors which start the lawlessness of the growth are such episodes as a scratch or laceration of the tumor, an infection, or crushing injury Even such factors as the multiple insults delivered by a wash cloth, the rubbing of a foot lesion by the shoe, the pinching of the collar band or belt, may be sufficient to precipitate the growth factor in a melanotic tumor which has previously been dormant

A child may have a congenital nevus which may grow only in proportion to the growth of the body as a whole The child may grow up and go through its entire life without the tumor taking on characteristics of lawless growth, even though it may be very cellular microscopically I have been much interested during the past 5 years in excising a number of melanomas for study, the removals being done during the course of other operations In the beginning I was greatly astonished to find many of them microscopically malignant Many quiescent melanomas are therefore malignant, but the one phase of lawless growth, the explosion, has not yet taken place

This thought brings us to the question of what should be done in the case of the congenital quiescent melanoma, and on this point one finds a wide divergence of opinion These opinions fall into 3 main groups the first group are those who feel that it is best to let a sleeping dog lie, these believe it is safer to gamble on the future of the tumor becoming a gangster rather than to disturb it. They are willing to take a chance on future scratches, rubbings, injuries, etc.

The second group is composed of men some of whom are dermatologists They attack the black mole with the electric needle For this type of therapy I have less than meagre regard In fact, I am convinced by the study of our 400 cases that the electric needle applied with good intent but without sufficient accuracy, is the one trauma responsible for as much wild growth as any other form of injury It is depressing to realize how frequently our patients give a history of having been perfectly well until the day he went for advice concerning his black mole, at which time electrodesiccation of the tumor was carried out. My objection to this technique is that it is impossible to know exactly when all the cells comprising the tumor are coagulated, and that too frequently a portion of the tumor is left unco-

agulated. Recurrence and mutation thus takes place as a malignant tumor from a tumor previously quiescent.

To the third group I claim allegiance. We believe that the best way to treat a quiescent melanoma is by simple, careful, scalpel excision, being cautious in going wide of the tumor in every direction, even going down to the fascia in most instances. One should exercise caution during the operation not to touch the actual tumor with forceps or knife. This treatment is good prophylactic cancer surgery and I have not witnessed any recurrences of the quiescent melanomas when this procedure is carried out.

Once having gotten under way in its full activity as a malignant tumor melanoma takes one or more of three courses First, it may grow locally invading the surrounding skin and subcutaneous tissues. Second, it may be disseminated to distant parts, being carried by the blood stream to the liver lungs, brain, spine etc. In this type of metastasis, usually no known therapy is of much avail. Third, metastasis may take place by way of the lymphatic channels to the nearest regional nodes, and it is in this type of extension that most of our cures come.

TREATMENT

There is no tumor which places the clinician in such a mental state of helplessness as the melanoma once it has left the original site.

The types of therapy in most general use are irradiation and surgery

1 *Irradiation* A considerable number of our 400 cases were treated by irradiation alone. This therapy was used in those instances in which the disease was far advanced, merely as a palliative measure. It was frequently employed about the face in positions in which a proper surgical operation would have been very mutilating Only rarely however was there a case in which the tumor completely disappeared. Melanoma occasionally responds like any other radiosensitive tumor Nine patients survived the 5 year period who were treated by irradiation as the complete therapy but of these 9 cases 3 patients are dead, 3 have disease present, and 3 are free of disease.

Our study of the results of irradiation therapy is very disappointing In those advanced cases in which palliation was most desired, irradiation failed. In fact it nearly always eventually failed We found that in only 2.5 per cent of our cases was there evidence of irradiation response. In other words, a melanoma is much more radioresistant than most other tumors Irradiation is, therefore, at the present time not to be considered proper treatment. We are disappointed to arrive at this conclusion because surgery very much needs a strong ally in this field. We do not stand alone in this viewpoint. Even such an aggressive protagonist for irradiation therapy as Ewing believes that, at the present time irradiation offers very little for the treatment of melanoma.

2 *Surgery.* In the absence of encouraging results from irradiation, we are left with surgery as our nearest approach to a method of combating this disease. The 400 cases covered by this report were admitted to the Memorial Hospital during the 18 years between 1917 and 1935 One hundred and fifty-five cases, or 39 per cent, were primary and 245 cases, or 61 per cent, were recurrent.

a. *Primary* Of the 155 primary cases, 50 were "primary advanced" cases in which no cure was to be anticipated. And in the 105 primary operable cases, it was deemed that there was an opportunity for cure. This means that of the total 400 cases studied only 26 per cent, or 1 in 4 cases has a fighting chance of cure.

In considering 5 year results, it must be stated that of these 105 primary cases, 70 patients were admitted prior to January 1 1931 We, therefore, have 70 primary operable cases on which can be reported the 5 year results of treatment. Of these 70 cases, 23, or 33 per cent, survived the 5 year period (Table I).

In these cases treatment consisted in surgery alone, and in some a combination of surgery and irradiation, reliance, however being chiefly on the surgical procedure

TABLE I.—38 CASES OF 5 YEAR SURVIVALS

	Primary	Recurrent
Total cases	23	15
Free of disease	18	5
Alive with disease	1	
Lost		2
Dead		8

b *Recurrent* Of the 245 recurrent cases, 141 were far advanced, and 104 cases, although recurrent, seemed to offer some opportunity of cure. Prior to 1931 100 cases were classified as advanced and 55 as recurrent operable Of the total 151 recurrent cases up to 1931 15, or 10 per cent, survived the 5 year period 8 of these however later died of disease (Table I)

Of the 55 recurrent operable cases prior to 1931 15 patients, or 27 per cent, survived the 5 year period and this figure, 27 per cent, compares favorably with the 33 per cent 5 year survivals of the primary operable group however not as large a proportion of these recurrent cases re-

maimed cured If one includes every case prior to 1931, no matter what group it falls in, there are 267 cases, and of these, there are 38, or 14 5 per cent, 5 year survivals

3 *Coley's toxins* In 15 cases here reported, Coley's toxins were used usually along with irradiation or surgery or both, but as no one patient of these 15 cases survived a 5 year period, it must be considered that it was used as a measure of desperation and obviously added nothing to effective therapy of melanomas

TABLE II —267 CASES TREATED PRIOR TO 1931

	Number	Per cent
Dead	165	62
Cured	33	12
Living with disease over 5 years	5	2
Lost	64	24

It is appalling that in 38 instances, or nearly 10 per cent, electrodesiccation of the lesion was employed

In 26 cases the disease was primary in the eye Melanoma of the eye has a rather typical course it survives for many years after the eye s enucleation, before manifesting itself in other locations It then usually appears at the liver In one instance there was a period of 25 years between the enucleation and the clinical signs of metastasis to the liver

Subungual and intra-ocular melanomas are probably the types in which best results are obtained by treatment On the other hand melanoma of the vulva, the intra-oral cavity, and the rectum are especially fatal

TRAUMA, A CAUSE

Melanoma is one of the rare forms of cancer in which there is a causal relationship between injury and the activation of a malignant process It is not to be inferred, however, that injury is the only cause of this activation The injuries reported were many and varied in type In one instance a hypodermic injection of typhoid vaccine was given through a quiescent mole, which immediately commenced its wild growth Numerous instances are given of the patient cutting a mole on his face while shaving

A factor of greatest importance is the duration of time which elapsed between the beginning of lawless growth and the treatment of the patient This averaged 2 years and 2 months Possibly such delay may be accounted for by the fact that the patient thought the lesion had been present for years, and therefore was still unimportant

SUMMARY

1 Melanoma is one of the most malignant of all malignant tumors

2 A fair proportion of 5 year cures can be obtained in early cases *if* a well planned operation is performed, and to do this the operator *must* go wide and deep The tendency is to excise too close to the lesion

3 The 5 year results of operation are 33 per cent for the primary operable and 27 per cent for the recurred operable melanoma However, the great majority of cases that present themselves are advanced, so that no therapy will produce a cure

4 The non-pigmented melanomas are commonly not diagnosed before operation They are usually, therefore, badly handled They have a high degree of malignancy, being usually grade 3 They are, however, commonly radiosensitive

5 Thirty-eight cases of 5 year survivals of melanoma are reported

6 Our best results in treatment take place when the melanoma is situated in the eye or beneath the nail, and our worst results are associated with disease in the vulva, the rectum, and within the mouth

7 Irradiation and Coley's toxins are of questionable value The only method of therapy to be employed is aggressive, exact, well planned and skillfully executed surgery

8 If we are ever to improve our results in the treatment of melanoma, it must come along the line of applying a common sense rule as to which moles to leave alone and which to remove In the removal of the mole containing black pigment as a prophylactic measure lies our chief hope of improving the percentage of patients cured More and earlier surgery should be employed, rather than less

THE TREATMENT OF PROSTATIC CARCINOMA[1]

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THE control of prostatic carcinoma presents one of the most difficult problems in the field of cancer Many urologists believe seriously that its control is impossible. While we acknowledge the difficulties, we believe that in a small number of cases they can be overcome.

Intelligent treatment of prostatic carcinoma presupposes an accurate conception of the pathological anatomy of the carcinoma with particular emphasis on the point of origin. Considerable confusion has arisen as to the exact lobe or lobes in which the cancer originates.

The examination of very small prostatic cancers found at autopsy clinically undiagnosed and undiagnosable, indicates that, in about 75 per cent of all cases, the posterior lobe of the prostate is the place of origin of prostatic cancer In 2 such cases, Young first reported small prostatic cancers originating in the posterior lobe Moore, in 52 autopsy cases, reports 75 per cent having origin in this lobe. In the 25 per cent remaining of all cases, the origin of the cancer may be in the lateral median or anterior lobes There may be multiple foci of origin.

When the prostatic cancer has become sufficiently large to be clinically diagnosed, in most cases it has extended beyond the posterior lobe into the lateral or median lobes and into the sheath of the prostate In 27 prostatic cancers small enough for radical resection, Young found but 1 case in which the posterior lobe alone was cancerous Randall, examining still more advanced prostatic cancers, dissented from the posterior lobe origin. There is considerable proof that the cancer may remain for a long time in the posterior lobe, that it may extend beyond the posterior lobe, the perivesical lymphatics, and the retroperitoneal glands without involving the median or lateral lobes. Reports are found in the literature of cases in which the median and lateral have been removed and showed no cancer but the patient finally succumbed from cancer originating in the posterior lobe.

ASPIRATION BIOPSY

The control of prostatic cancer depends upon the diagnosis of the carcinoma in its early stage Aspiration biopsy through the perineum has been a great help in the diagnosis of such cases. One succeeds in obtaining prostatic tissue in about 80 per cent of the cases which are aspirated. The pathological diagnosis of this aspirated specimen depends upon special training on the part of the pathologist. Tissue may be aspirated easily from the posterior lobe but it is more difficult to obtain from the median and lateral lobes.

ANATOMY OF THE PROSTATE

A study of the anatomy of the normal prostate shows it to have the shape of a somewhat flattened cone with its base at the bladder end and its apex downward along the urethra. The entire prostate is below the bladder and this posterior lobe, which is the source of origin in so many cases, begins one half inch below the bladder neck, a position which makes difficult the proper irradiation of the lobe by the implantation of radon seeds through the bladder opened suprapubicly

OPERATIVE CONTROL

Progress in the operative control of prostatic carcinoma has been slow A study of the cross section of the prostate reveals how small the field of operation is. Operative removal presupposes much trauma to the cancerous tissue. Trauma, following Ewing's dictum, is the greatest factor in dissemination of the cancer One of the earliest changes in prostatic carcinoma is "perineal invasion of the prostatic capsule" (Moore) Invasion of the vesicles and distant lymphatic invasion, however is a late manifestation. This fact might be construed as favoring either operative removal or irradiation treatment. Young, who originated radical resection reports the cases of a few patients operated upon and very few 5 year cures. No other urologist shows even comparable results.

TREATMENT BY IRRADIATION

Irradiation offers the only hope to control these difficult cases, and irradiation means the combination of deep X ray therapy and intraprostatic irradiation. We have sufficient proof that neither of these alone is enough to control the disease Deep X-ray therapy and intraprostatic irradiation should be administered simultaneously as far as possible. Our present conception of the proper way to apply deep X-ray therapy (200 kilovolts) is that it should be given through 5 portals of entry 300 r being given daily at a distance of 70 centimeters until 1550 to 1900 r or even more are given to each portal.

[1] Presented at the Cancer Symposium before the Clinical Congress of the American College of Surgeons San Francisco October 26-November 1 1935

TABLE I —PROSTATIC CANCER CASES CONTROLLED

	Total cases	Cases	Per cent
First series	46		
Radiation of prostate alone—no external irradiation—well 5 years		5	10
Second series	351		
Too extensive for treatment			20
Irradiation of prostate alone—no external irradiation—controlled 3 years		29	8 3
Controlled over 5 years		20	5 7

TABLE II —SIZE IN 322 NON-CONTROLLED CASES

	Cases
Extensive	294
Medium	19
Small	9
Total	322

TABLE III —SIZE IN 29 CONTROLLED CASES

	Cases
Extensive	15
Medium	7
Small	7
	29

TABLE IV —TIME FROM WHEN FIRST SEEN TO DEATH IN 322 NON-CONTROLLED CASES

	Cases
1 to 6 months	91
6 to 12 months	72
12 to 24 months	80
2 to 3 years	32
3 to 4 years	12
4 to 5 years	3
5 years	3
? years	29
Total	322

The usual portal is 10 by 12 centimeters External irradiation as a rule is not repeated Intraprostatic irradiation is carried out by means of radium If the posterior lobe alone is involved, removable radium needles, gold screened, are inserted into the prostate through the perineum, 1500 to 1800 millicurie hours are given intraprostatically every 2 months until the carcinoma of the prostate and of the periprostatic region is controlled If the lateral and median lobes are involved, suprapubic implantation of radon seeds is the treatment of election The seeds, having a dosage of 1 5 millicuries, are implanted throughout each cubic centimeter of prostatic tissue One

TABLE V.—TIME WELL IN 29 CONTROLLED CASES

	Cases
3 to 5 years.	9
5 to 10 years	16
More than 10 years	4
Total	29

TABLE VI —DIAGNOSIS IN 29 CONTROLLED CASES

No pathological diagnosis	14
Pathological diagnosis	15

1 Carcinoma (aspiration)
2 Adenocarcinoma
3 Adenocarcinoma grade 1 radioresistant.
4. Carcinoma probable not positive (aspiration)
5 Adenocarcinoma—some infiltration grade 2
6 Papillary carcinoma of bladder—secondary to prostatic carcinoma
7 Adenocarcinoma grade 2 radioresistant
8 Carcinoma (diagnosis from previously removed prostatic tissue)
9 Infiltrating carcinoma grade 3
10 Probably small cellular carcinoma (aspiration)
11 Carcinoma (diagnosis from previously removed prostatic tissue)
12 Carcinoma (diagnosis from previously removed prostatic tissue)
13 Carcinoma (diagnosis from previously removed prostatic tissue) At Memorial (Ewing) prostatitis beginning precancerous changes
14. Carcinoma (diagnosis from previously removed prostatic tissue)
15 Adenocarcinoma (diagnosis from previously removed prostatic tissue)

may not be able to implant the posterior lobe from this approach, in which case, perineal needles are inserted, as just described

The treatment of retention is by means of transurethral or suprapubic partial prostatectomy with the high frequency loop This operation is followed by irradiation in accordance with the technique outlined Modifications of the operation and the irradiation dosage must of necessity depend upon the conditions found in the patient treated

A study of 351 consecutive cases of prostatic carcinoma gives an idea of what even inadequate irradiation of the prostate alone can accomplish (Table I) The series in which adequate external and intraprostatic irradiation has been used, is not yet ready to report

It is interesting that more than one-half of the cases controlled were classified as extensive (Table III), that is, the growth extended beyond the prostatic sheath and involved the bladder base or the perivesical lymphatics.

Table IV shows that the large majority of patients who are to die, succumb in the first 2

years. It is interesting that 3 patients lived more than 5 years.

Table V shows that 29, about 8.3 per cent, were well for 3 years and 20 5.7 per cent for 5 years. A patient in whom the carcinoma is considered as controlled must have no signs of carcinoma in the prostate, by palpation by cystoscopy or by aspiration biopsy. This is also true of the skeletal and other parts of the body which might be affected by the carcinoma.

The fact that the X-ray revealed metastases in 156 cases and that of these 44 or 28 per cent, showed metastases to bone indicates how serious is the problem of control.

Table VI shows the importance which aspiration biopsy plays in the diagnosis. In 3 cases the diagnosis was confirmed by this method.

I have touched not at all in this paper upon the treatment of incurable neoplasms, particularly those with metastases to bones and around nerves. That is a problem in itself. The statistics I have quoted might well lead to pessimism in the outlook for cancer of the prostate. I believe however that with pains, intelligence and often infinite patience in treating these patients, we can optimistically predict that future statistics will show at least 100 per cent improvement in our figures.

TREATMENT OF CANCER OF THE UTERINE BODY[1]

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IN estimating the comparative effectiveness of radiation and of surgical attack, radiosensitivity of the growth in question is obviously of primary importance. There has by now accumulated sufficient experience to justify classification of many of the important types of cancer with regard to degree of radiosensitivity. Stewart has published an extensive review of the literature on this subject with comment based on experience at the Memorial Hospital. Corpus carcinoma appears to be but slightly radiosensitive with the exception of a small group (12 per cent) of highly anaplastic very malignant growths (grade 4 type).

Nevertheless, as Stewart points out, radiosensitivity may be quite different from radiocurability. The effectiveness of radiation therapy depends, as well, on other factors than radiosensitivity not the least important of which is accessibility of the growth to concentrated, very large doses of radiation. If it is possible to utilize the caustic effects of radiation even low radiosensitivity may not prevent destruction of the growth. This accessibility is true of endometrial growths confined in and protected by a thick walled uterus. Therefore even theoretically it is quite possible that fundus carcinoma, though relatively radioresistant, may nevertheless be radiocurable. It is necessary to seek the answer in clinical experience.

Three years ago the Cancer Commission of the California Medical Association[1] undertook the standardization of cancer therapy in so far as it was considered possible so to do. This was carried out by the method of consultation of physicians experienced in all fields of treatment concerned. Committees were formed to survey each type and location of cancer; committees constituted of surgeons, specialists, radiologists, pathologists, internists, numbered over 300 members. Before the final report of each committee was accepted by the Cancer Commission it was submitted to all members of all committees. This has been, we believe, the first attempt to collect and set forth the experience and opinion of the entire profession rather than of individuals or of individual groups or even of the men engaged in any one branch of therapy. It resulted in a highly illuminating and significant volume of data covering practically the entire field of malignant disease therapy.

The Committee on Gynecological Tumors, of which Dr. E. N. Ewer was chairman made this statement in its final report, approved by the Commission: "In adenocarcinoma of the body there is a feeling that panhysterectomy is sufficient without dissection of the parametria and that if there is any parametrial infiltration the case should be handled with radium and deep X-ray. Surgery has been so successful in this class of corpus cancer that the committee is slow to advise any change to radium and X-ray but it must be admitted that these agents are also very reliable and can be used with much confidence when surgery is contra-indicated. All cases for which surgery is selected should receive, if

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possible, full radium and X-ray radiation 6 weeks before operation"

A substantially similar statement is contained in the report of the Radiology Committee

Briefly, then, the Cancer Commission recommends hysterectomy with pre-operative radiation in cancer limited to the uterus, and radiation therapy in cancer extending beyond the wall of the organ

Turning to the literature of 1933 and 1934 (since publication of the Cancer Commission reports), Zweifel collected a group of statistics from other authors and found the average reported percentage of 5 year cures after surgery appreciably higher than after radiation therapy alone, but found the highest percentage of cures when both radiation and hysterectomy had been employed Of 19 authors reporting during this period, 10 employ hysterectomy and 9 depend on radiation therapy Of those who do hysterectomy, the majority state definitely that their cases are selected either on a basis of histological grading, of clinical invasion outside the uterus, or of high operative risk In cases not regarded as favorable for operation, radiation is used exclusively This is substantially the position of the Cancer Commission, outlined above, and there appears, therefore, no good reason yet to abandon it

In making recommendations before an organization such as the American College of Surgeons, whose members work, for the most part, in general hospitals throughout the country, the factor of availability of equipment and personnel is a very important one The retiring president of the College himself one of the foremost students of cancer in America, has pointed this out in a recent address (6) from which I take the liberty of quoting

> Radiotherapy has developed to the stage where it is the method of choice for the treatment of common and important forms of metastasizing cancer, such as cancer of the cervix, even in its early stages But, while this development of radiotherapeutics, as practiced in the great cancer institutes and hospitals is continuing day by day, the equipment for providing radiation in adequate amount and the personnel trained to its effective use cannot be so readily or so promptly made available Cancer institutes and special cancer hospitals are unable to supply treatment for more than a very small fraction of the 300,000 cancer patients living in this country in any one year
>
> Under these circumstances, the majority of patients who have cancer will be obliged to seek treatment as they have in the past, in general hospitals and at the hands of surgeons and radiotherapists who are not attached to the great cancer institutes and are not equipped with the most efficient apparatus or trained in the advanced technique of radiation therapy
>
> We are forced to consider the different standards of diagnosis and treatment of cancer which are obtainable in different localities and to make the best possible use of the resources which are available for this purpose Such a plan involves consideration of the indications for the selection of radium and X-ray treatment or of surgical measures in the treatment of individual cases, in so far as this choice may be restricted by the fact that one or another of these methods of treatment and the personnel qualified to administer such treatment may be available or be lacking in the locality under consideration.

It cannot be too strongly emphasized that successful radiation therapy for cancer requires a very high degree of technical skill and training, as well as the exercise of judgment and even of courage, comparable with these qualities as we have come to expect them in the competent surgeon Even the dosage required for modern successful radiation therapy is such as to be approached with trepidation by the man whose experience and standing in this special field will not withstand criticism for unfavorable by-effects Percentages of cures reported in the literature from large cancer services by no means present a picture of the results obtained generally by less experienced therapists For example, the newly formed cancer committee of one of our large hospitals undertook to ascertain end results in some 50 cases of cancer of the cervix treated in that hospital up to 5 years previously and found not a single one living

It is probably safe to state that more communities have surgeons competent to do a good hysterectomy than have radiologists and equipment adequate for the effective radiation treatment of fundus cancer

CONCLUSION

While there is good authority for the use of radiation therapy exclusively for fundus cancer, it appears that the weight of clinical experience favors hysterectomy, preferably with pre-operative radiation, at least for cancer still confined to the body of the uterus Especially is this true in the absence of available radiation therapy comparable to that of the large cancer clinics For the small group of extremely anaplastic and highly malignant cancers and for cancers which have already extended beyond the wall of the uterus, radiation therapy is in any case the method of choice

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THE TREATMENT OF CANCER OF THE COLON[1]

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THE attack against cancer has been wrought up to such a pitch that the army is prone to attack the foe before the best time is at hand —and there is, after all, an optimum time This is particularly true in cancer of the colon and rectum Operative intervention in the presence of cancer of the colon is practically never an emergency procedure, the only exception being in the occasional acute obstruction superimposed on the napkin-ring type of malignancy in the sigmoid However, operations for malignancy upon the gastro-intestinal tract carry a very high mortality unless the diagnosis is accurate, the patient properly prepared, and the operative procedure properly planned beforehand

Malignancies of the right side of the colon are rarely obstructive in nature, due to the liquid nature of the contents, large lumen of the bowel, and flat growths, therefore, as much time as is necessary should be taken to rehabilitate the patient with such measures as high caloric diet, iron, glucose and saline infusions and transfusions In growths of the right side, the associated presence of anemia is not as bad a prognostic sign as is malignancy of the stomach or of the sigmoid, because these generally signify metastatic growths Anemia on the right side of the colon, however, is generally due to physiological disturbances Excision of the growth with anastomosis on the right side of the colon is a dangerous procedure because of the blood supply, and it will result in few cures, due to poor removal of the lymphatic glands In all growths of the right side, it is necessary as well as simpler to remove the entire ascending colon including the hepatic flexure, and to do an anastomosis between the ileum and the transverse colon either in one or two stages, depending upon the general condition of the patient and the experience of the surgeon If operation is performed in two stages, I believe that the end-to-side anastomosis, as Rankin has so ably demonstrated, should be carried out in order completely to divert the contents of the small intestine, because if the side-to-side anastomosis is made, considerable contents will still pass over the growth If, however, the one stage operation is performed, side-to-side anastomosis may be made

When the growth is situated in the transverse colon, I prefer to do a cecostomy, and 2 or 3 weeks later resect the growth and do an end-to-end anastomosis Here, again, the Rankin clamp is useful, care being taken, of course, to pay attention to the blood supply In certain cases, one could readily perform the obstructive resection type of operation as devised by Rankin if he so chooses, but many of these necessitate secondary closure This same procedure is applicable to growths in the descending colon and sigmoid, although if the growth is in the lower end of the sigmoid, a sigmoidostomy above the growth will prove more efficacious for decompression of the bowel than will cecostomy This is true because many of these patients have been constipated for many weeks or months and considerable fecal material has accumulated in the transverse and descending colon which would be difficult to remove by cecostomy Resection of the sigmoid is a very dangerous procedure without some type of decompression and probably should seldom be carried out in a one stage operation, unless the lesion is very small and unless there is no obstruction above the growth or dilatation of the bowel below the growth The Mikulicz procedure, in my experience, has been of little usefulness because it can be utilized in such a small percentage of cases

Operations upon the colon have been fairly well standardized, but there has been great controversy regarding the most satisfactory operative procedure for malignancy of the rectosigmoid and the rectum Many different types of operations have been devised, chiefly because of the desire to retain in some way the sphincteric apparatus, but in the final analysis of these various procedures, it is quite apparent that the disease being treated has often been lost sight of in the effort to maintain sphincteric control Many ingenious operations have been designed to restore the lumen and this may be done perfectly well technically, but the possible curability is lost sight of due to the fact that it is the generally accepted belief that cancer of the rectum remains localized for such a long time When one looks over the reports of the number of patients cured, this does not necessarily follow Cancer of the breast may oftentimes remain *in situ* for 2 or 3 years but nevertheless, its dangers are not minimized

I feel that a great error has been made in performing small operations for small cancers and big operations for big cancers From our conception of the disease and judging by the frequent number of recurrences, perhaps the opposite procedure should be carried out. After a very large

[1]Presented in the Cancer Symposium before the Clinical Congress of the American College of Surgeons, San Francisco, October 28–November 1 1935

experience with carcinomas of the rectum and a study of the locations of recurrences, Miles has given us the most lucid description of the lymphatic distribution, which is the chief mode of spread in cancer of the rectum or rectosigmoid. He concludes from this study that the most radical operation is the procedure of choice. Objections to this have always been brought up due to the occasional patient who is cured by a limited procedure but if this plan were followed in all cases, a very low percentage of cures would result. Therefore we have particularly favored the one stage combined abdominoperineal operation as that which gives the most hope for eventual cure.

I think that perhaps too much attention has been paid to operative mortality when a decision is made regarding which type of operation is to be used. The advantages of a 10 per cent mortality over a 15 per cent mortality in any procedure may oftentimes be misleading, unless we know the types of cases which are operated upon and the surgeon's ability to carry out the procedure. Operability varies greatly with the experience and courage of the surgeon, but certain it is that an abdominoperineal operation, whether done in one or two stages increases the ratio of operability. We have favored the one stage abdominoperineal operation for many reasons. In the first place, we are operating upon the patient once instead of twice, and when one considers accidents beyond our control, the mortality of the combined first and second stages is higher than is apparent, because the mortality from this operation is not quoted unless the patient goes through the second stage. If he dies in the first stage death is automatically counted as due to colostomy and not to cancer of the rectum. In the second place, the operation is more easily performed without the presence of adhesions from the previous operation and it can be performed more expeditiously and with less shock. Third, the period of hospitalization is considerably lessened. My own experience has been that, if a growth is inoperable at the first operation it is generally inoperable at the second operation.

In the patients who come in without an acute obstruction, we feel that we can decompress the bowel in practically all cases, if a proper regimen is instituted and sufficient time is allowed. This usually consumes about a week. We use 1 ounce of magnesium sulphate to 8 ounces of water and have the patient take this over a 4 hour period each morning for many days. Cleansing enemas are also given every day and a few doses of pitressin are administered. During the hospital stay the kidney function is estimated and if there are any symptoms of disease of the bladder cystoscopy is done to estimate the size of the prostate or any invasion of the bladder wall by malignancy. Many of these patients are between 55 and 65 years of age and frequently have an associated prostatic hypertrophy which may be troublesome in the postoperative convalescence if it is not recognized. Blood counts are checked and transfusion is resorted to whenever indicated. The patient is given a high caloric, non-residue diet which includes candy, glucose, orange juice, etc. On the day before operation, all laxatives are discontinued, and proctoscopic examination is made to be certain that the rectum and the sigmoid are clean.

In our hands, spinal anesthesia has proved to be the one of choice because it provides excellent relaxation and a quiet abdomen. The patient is placed in extreme Trendelenburg position so that the pelvis is entirely free from the intestines. This requires a minimum of trauma in packing off the intestines. First the liver is explored for metastases, then the gland-bearing area, and finally the growth itself, the latter being done very carefully. Palpable glands do not preclude operation and neither does a moderate amount of fixation.

The first step in the operation is to mobilize the sigmoid in cases in which it is necessary, due to peritoneal folds on the lateral side. Then we isolate the inferior mesenteric artery and ligate it just below the first sigmoid branch. This is readily detected by the use of a Cameron light in case of a thin mesentery and, in case of a thick mesentery it is located by incising the peritoneum of the mesosigmoid 2 inches below the bifurcation of the aorta and back close to the promontory of the sacrum. This eliminates practically all bleeding.

The peritoneum on either side of the mesosigmoid is then incised down to the bottom of the pelvis, and these membranes are joined on the anterior wall in the rectovesical pelvis in the male, or in the pouch of Douglas in the female. The hand is then placed at the promontory of the sacrum, and all the fat in the mesosigmoid in the hollow of the sacrum is pushed forward, and the dissection is carried down until the coccyx is felt. Then the rectum is dissected free anteriorly, the seminal vesicles being pushed forward until the upper border of the prostate is felt. Traction on the bowel will then bring into view the lateral attachments of the rectum which are cut. This may be done posteriorly but if done anteriorly it greatly facilitates the perineal part of the operation. The peritoneum is then dissected from

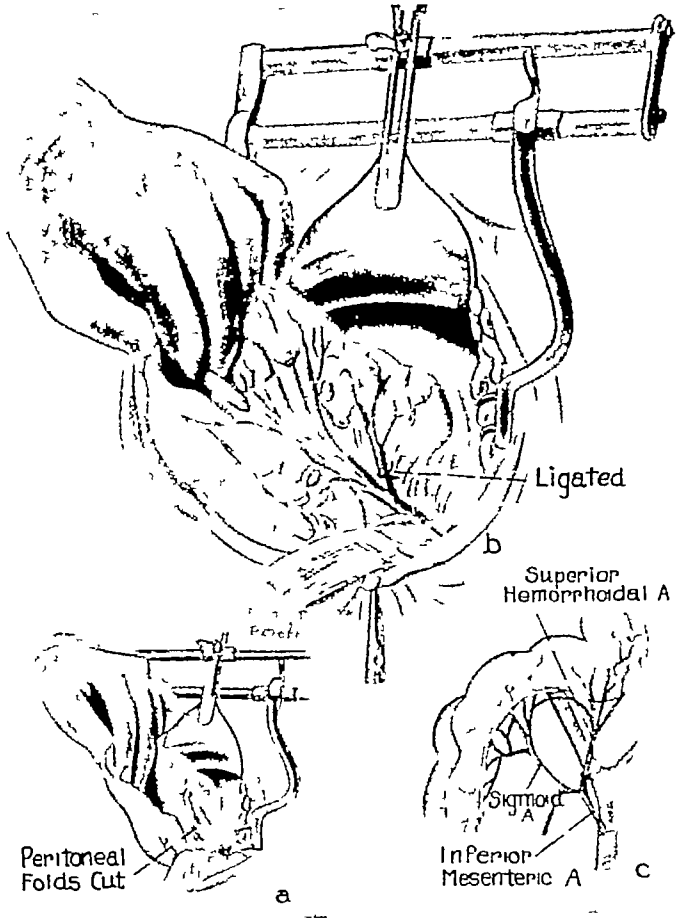

Fig 1 a, Mobilization of sigmoid, if necessary by division of peritoneal attachments which may be present on lateral side. b, Inferior mesenteric artery identified and ligated below first sigmoid branch. c, Blood supply of rectosigmoid

the lateral walls of the posterosuperior surface of the bladder in order to reconstruct the pelvic floor The bowel is then divided as the last step in the procedure because, should contamination occur accidentally, it will not be of any consequence inasmuch as all the dissection has been completed

The bowel is then divided with cautery between two Payr clamps and each end is tied firmly with a heavy silk ligature Over each end is placed a square piece of rubber dam which is again tied over the bowel This is very much quicker and much less apt to cause infection than inversion of the stump with a ligature The distal end is pushed down into the pelvis The pelvic floor is reconstructed with the flaps of peritoneum, under no circumstances should it be under tension After all available peritoneum has been used, if there still remains a hiatus, it should be covered over with an omental graft In the female, the uterus is used in the reconstruction of the pelvic floor The proximal end of the bowel, if long enough, is brought out in the midline at the site of the abdominal incision as a permanent colostomy If the sigmoid loop is short, it is brought out through a left McBurney's incision. It is my observation that people with midline colostomies are better satisfied than those with left inguinal colostomies because when they are dressed, the abdomen looks symmetrical If a colostomy bag is worn, it fits better than a left inguinal colostomy which frequently rides the crest of the ilium, is

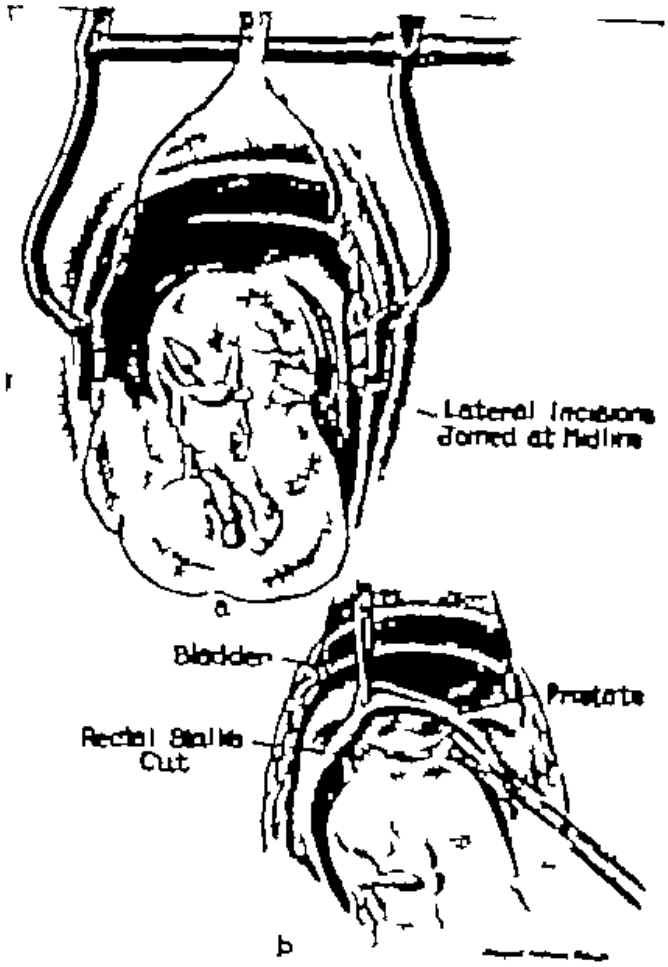

Fig 2.

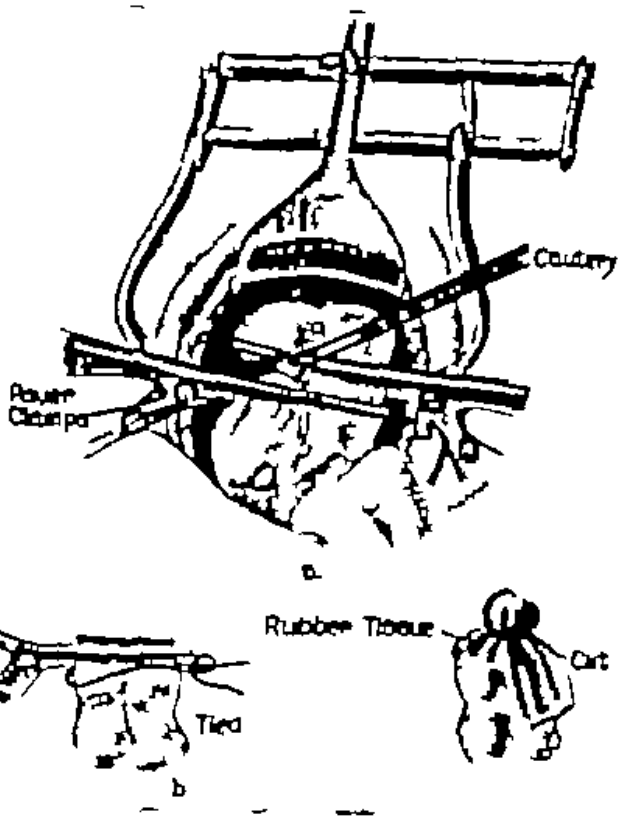

Fig 3

Fig 2 a, Incisions in peritoneum on both sides of mesosigmoid until they meet anteriorly in the rectovesical pouch in the male, or in the pouch of Douglas in the female b, Bladder and seminal vesicles pushed forward to point where prostate can be felt—traction on bowel then renders prominent the rectal stalks which are cut

Fig 3 a, Bowel divided between clamps and cut with cautery b, Ends of bowel tied c, Ends of bowel covered with rubber dam and tied again

Fig 4 a, Distal end of bowel pushed down into pelvis b, Closure of peritoneum (floor of pelvis) c, Closure of muscle layer d, Abdomen closed—proximal end of colon brought out for permanent colostomy

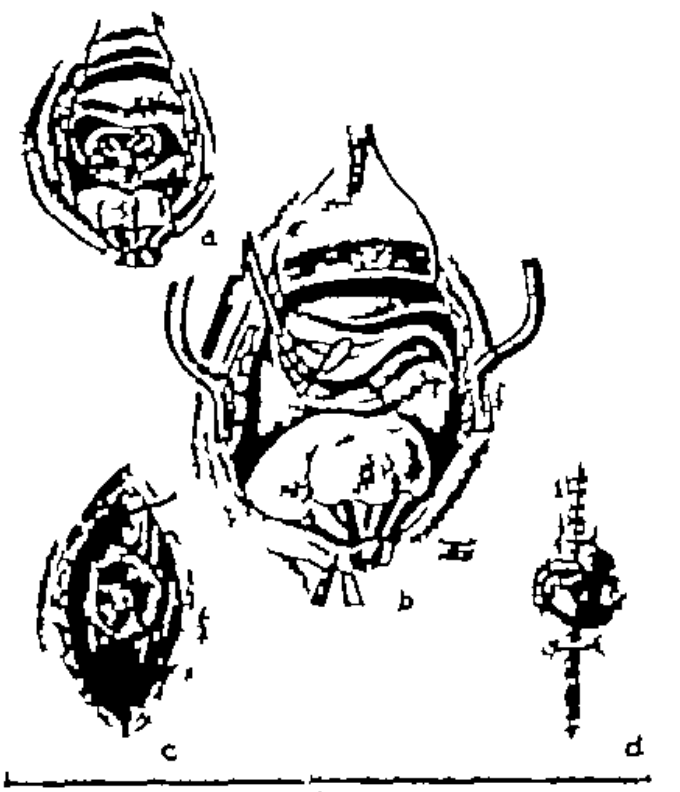

Fig 4.

decidedly uncomfortable and, frequently leakage occurs. The colostomy is not stitched to the peritoneal fascia or skin because with peristalsis, the stitches will pull out and thus cause a weak spot in the bowel wall through which the mucosa will blow out and cause peritonitis or severe infection in the abdominal wall. There frequently are enough appendices epiploicæ left on the bowel to rest comfortably on the fascia or the skin, which, if snugly sewed around the bowel, will prevent its slipping back. In not a single case in our series has a suture been used and in no case has it slipped

The patient is then turned on the abdomen and placed in the Kraske position A purse-string suture is placed around the anus, and a midline incision is made from the lower end of the sacrum

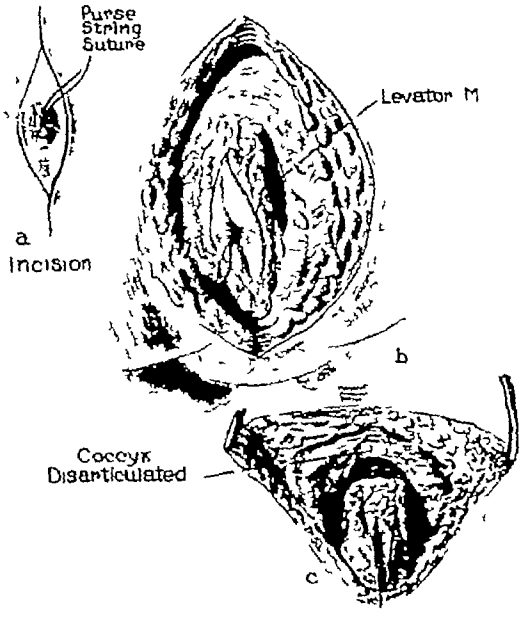

Fig 5 a, Pursestring suture about anus Midline incision b, Flaps dissected back to edge of gluteus muscle c Coccyx disarticulated from sacrum and fascia beneath it incised.

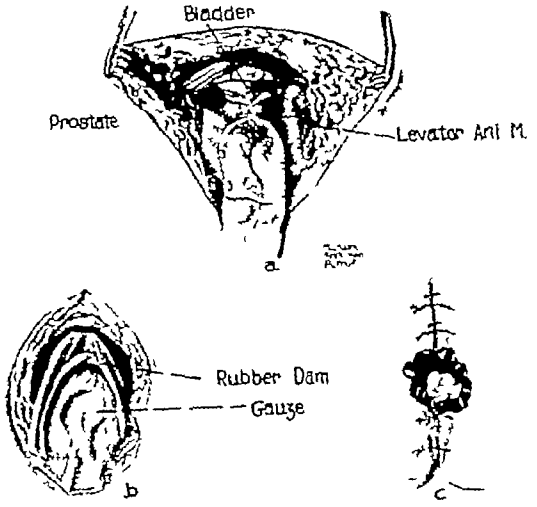

Fig 6 a, Incision in presacral fascia exposes bowel cavity containing bowel removed from above downward b, Large square of rubber dam placed in cavity—gauze packed in dam so that it does not adhere to new pelvic floor closure. c, Closure.

to the perineum encircling the anus If the growth is low lying, more peri-anal skin is removed than when it is located higher up Flaps are dissected laterally until one encounters the gluteus maximus muscle, and all the structures including the ischiorectal fat are displaced medially The coccyx is then disarticulated and the presacral fascia incised, thus bringing into the operative field the cavity containing the distal end of the cut off sigmoid This is pulled out and dissection of the rectum is done from above downward rather than from below upward It is a simpler procedure and is attended by less bleeding It must be remembered that an incomplete abdominal dissection renders the posterior operation more difficult

There remains then, a very large cavity surrounded only by the walls of the pelvis and the bladder anteriorly, and into this cavity we place a large square rubber dam and pack gauze into it, the rubber dam preventing the gauze from adhering to the new pelvic floor which may be torn when the gauze is removed This large pack helps to support the new pelvic floor and, by its pressure on the surrounding structures, it also prevents oozing Part of this gauze is removed on the third and part on the fourth day after operation, after which the cavity is irrigated daily with care to prevent infection The colostomy is opened on the second or third day according to the amount of distention Formerly, we used a retention catheter for 4 or 5 days, but recently we have not resorted to this unless necessary We feel that bladder irritability and cystitis have been minimized by this new procedure Treatment from this point is symptomatic, and we encourage the patient to be out of bed on the twelfth to the fourteenth day because this helps the new pelvic floor to sag, thereby filling in the posterior cavity a little sooner than it would if the patient were in bed for a longer time

The one stage combined abdominoperineal operation is admittedly a severe one, but it is not intrinsically difficult nor does its performance demand exceptional ability However, it is not merely a technical maneuver The surgeon must assume responsibility for meticulous pre-operative preparation He must plan the operation well He must direct good postoperative care and finally instruct the patient in the management of the colostomy which is so essential to comfort The results of this well rounded-out plan have been gratifying In a personal series of 151 cases, there have been 16 deaths, a mortality of 10 5 per cent. Fifty-two per cent of the patients are living and well for 5 years, 62 per cent for 3 to 5 years, and 70 per cent from 1 to 3 years

TREATMENT OF CARCINOMA OF THE LARYNX[1]

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In selecting surgical methods for the treatment of carcinoma of the larynx, definite technical procedures should not be decided upon before operation, except in a limited group of cases in which the growth is well defined. Rather, an exploratory operation should be undertaken first and the surgical procedure that seems best suited to the individual case should then be employed. This selection should depend on the situation of the growth its extent and type and on the patient's age and general condition. While the voice must be conserved whenever possible eradication of the disease is of the greatest importance. In cases in which small early growths involve the anterior part of one vocal cord thyrotomy and removal of the growth is unquestionably indicated. In cases in which there are more extensive tumors of the epiglottis and aryepiglottic fold, pharyngotomy and removal of the growth is indicated, and for still more extensive laryngeal growths laryngectomy should be performed.

CLASSIFICATION OF TUMORS

The usual classification of carcinomas of the larynx into intrinsic and extrinsic growths, depending on whether they involve the vocal cords and adjacent part of the larynx or whether they extend out over the rim of the arytenoid region or aryepiglottic fold is of little value in determining operability in these cases or what procedure should be followed in removing the growths. It is well known that growths originating on the vocal cord anteriorly, tend to grow much slower and to metastasize late owing to the lack of lymphatic drainage. These have been called intrinsic tumors. Growths of the epiglottis and aryepiglottic fold have been called extrinsic tumors and it is usually believed that these tend to metastasize early and that the prognosis is usually much worse for them than for the former. However while this may be true at times, growths of the epiglottis and aryepiglottic fold often are of a low grade of malignancy and regardless of their position they tend to metastasize very late if at all while a carcinoma of a high grade of malignancy on the vocal cord may tend to metastasize early.

The general classification of laryngeal tumors into intrinsic and extrinsic therefore forms a basis for discussion. But it is not in this manner one considers them in determining the best treatment in the individual case. The growth, which may appear entirely intrinsic may extend through the thyroid cartilage or the cricothyroid membrane or above the rim of the thyroid cartilage. In about 17 per cent of the cases in which it is necessary to perform laryngectomy the growth has perforated through the thyroid cartilage or the cricothyroid membrane. It is impossible at times to determine this extrinsic involvement by palpation, by roentgenological examinations, or by any other method.

From the standpoint of methods of removal, growths of the larynx may be divided into 3 groups (1) supraglottic tumors, (2) intralaryngeal tumors, including subglottic growths, and (3) laryngopharyngeal tumors, those arising in the pyriform fossa and posterior wall region. Many of these growths however may involve 2 or possibly all of these regions so that definite anatomical divisions cannot be made.

METHODS OF SURGICAL TREATMENT

In determining the method of treatment for any laryngeal lesion the question of the type of carcinoma is very important, and, unless one can remove the growth in a conservative way with a sufficiently wide margin as brought out by New and Fletcher then a more radical procedure should be followed. Surgical procedures, including excision and surgical diathermy are the most effective methods of treating carcinoma of the larynx. In the treatment of tumors of a high grade of malignancy irradiation used before and after operation seems to be of additional value.

Supraglottic tumors. Growths in the supraglottic region may produce few if any symptoms until they are of quite large size. Growths of the epiglottis of a low grade of malignancy may cause difficulty in swallowing as their first symptom. Sometimes an indeterminate ache or pain in this region may bring the patient for examination. Until these growths have extended into the larynx hoarseness is not a symptom.

Tumors of the epiglottis of a low grade of malignancy are best taken care of when the lesion is definitely limited to the epiglottis by performing preliminary tracheotomy. Then by means of a Lynch suspension apparatus with a flat spatula, the growth may be removed under direct vision,

[1] Presented in the Cancer Symposium, before the General Congress of the American College of Surgeons San Francisco October 31 November 1, 1941

a protected diathermy point being used This particular method, however, should be limited to cases in which there is no question that the growth can be removed in this manner In cases in which the growth extends laterally to the aryepiglottic fold and the arytenoid region, subhyoid or lateral pharyngotomy is a better procedure The question whether to perform pharyngotomy through the thyrohyoid membrane after division and retraction of the hyoid bone or lateral pharyngotomy must depend on the situation and extent of the lesion In this way wide exposure can be made and as radical an excision performed as is necessary In these cases a window may be removed from the thyroid cartilage on the uninvolved side, in this way sufficient exposure can be obtained and the growth can be destroyed through this opening on the opposite side of the larynx The transmandibular and translingual exposure as used by Trotter to remove an epiglottic growth, we believe, has a very limited field The other methods are far more efficient, and from them the patient will receive less general reaction

Growths of the epiglottis occur more frequently on the posterior surface, and epitheliomas are the most common of the malignant tumors A fibrosarcoma may occur in this region, and it is best removed by destroying it under suspension, by surgical diathermy following preliminary tracheotomy

Carcinoma of the epiglottis may fill almost the entire hypopharynx, so that only a margin of the larynx is visible This type of growth, however, tends more to be an excrescence, appearing like a cauliflower that has gone to seed, and it may have a fairly limited attachment The treatment of this type of growth, of course, must be entirely different from that employed when the growth is infiltrating With supraglottic tumors of a low grade of malignancy, one is justified in being fairly conservative because of the fact that in these cases, if it is possible to remove the growth, the patient has a good speaking voice

Carcinoma of the epiglottis may extend not only onto the aryepiglottic fold, but into the pyriform fossa and lateral wall of the pharynx, so that laryngectomy together with removal of tissue involving the pharynx may be necessary As has been said, it is essential that the technical procedure to be followed should not be definitely determined before the tumor has been explored, as extension may frequently be found which would have been impossible to determine before operation These epiglottic growths may also extend to the postcricoid region

Intralaryngeal tumors Growths of the glottis cause hoarseness as an early symptom so uniformly that adult patients who are hoarse over a period of a month should be carefully examined to make sure that the hoarseness is not due to a malignant condition In examining such patients, various types of so called precancerous lesions are found, such as thickened leucoplacias, and so forth In cases in which the leucoplacia is markedly thickened, we feel that wide excision of the lesion by means of thyrotomy is advisable. Biopsy should not be made because it may show a benign condition and the patient then feels that removal is not essential On the contrary this type of condition is potentially malignant and the lesion should be removed widely There is a very small group of these precancerous lesions, however, that may be removed by means of suspension laryngoscopy In general, however, the larger lesions of this type are better widely removed and the base destroyed with surgical diathermy by means of thyrotomy

Malignant lesions in the region of the vocal cords may be taken care of in 4 ways Those involving the anterior two-thirds of the vocal cord without fixation may be removed by means of thyrotomy, with excision of the growth and destruction of the base by surgical diathermy Those involving the same region but with such fixation that the growth has not perforated through the thyroid cartilage may be removed by means of thyrotomy, the growth being removed along with the cartilage and the tissue being destroyed by surgical diathermy Growths in the anterior commissure are best taken care of by division of the hyoid bone, the opening being made through the thyrohyoid membrane In this way a careful examination can be made as to the exact extent of the growth In the treatment of tumors of a low grade of malignancy, thyrotomy is performed, with removal of the diseased tissue which frequently involves the anterior portion of both vocal cords and the anterior commissure This method was suggested by Jackson and is very efficient in the care of tumors of a low grade malignancy In the treatment of more extensive tumors with fixation involving the anterior commissure and the false cords, laryngectomy is done, preliminary tracheotomy is done first and then, as a secondary procedure, the larynx is removed from below

When laryngectomy is done, we use paravertebral anesthesia, and we prefer the midline incision We then divide the hyoid bone and retract it laterally with rake retractors The larynx is freed up from the muscles, first on one side and then on the other On account of the possible

extension of the growth through the thyroid cartilage or the cricothyroid membrane, it is essential that this dissection be made very carefully. If there is any question of extrinsic involvement at this point wide excision, either with a knife or cautery is advisable. The trachea is cut across below the growth and procaine is then injected into the posterior wall of the larynx and trachea. If the extent of the growth will permit, a tongue like flap of mucous membrane and submucous tissue is dissected free from the posterior wall of the cricoid cartilage leaving it attached to the tracheal mucous membrane. This aids in closure of the skin to the trachea. It is necessary to inject some procaine into the pharynx after the trachea has been cut across, as it is difficult to block this area with paravertebral anesthesia.

Dissection is then carried up onto the posterior wall of the larynx. The pharynx is opened, and in cases in which there is some question as to the posterior extension of the growth, exploration is made with the finger at this time. The larynx is then removed. The opening into the pharynx is closed with 2 layers of fine chromic catgut sutures. The trachea is sutured to the skin by means of silk sutures. One mattress suture just above the trachea is carried through the anterior wall of the esophagus in order to bring it forward against the skin. Mattress sutures are used in closing the lower 5 centimeters of the skin above the trachea. Rubber cigarette drains are carried into the pockets on either side and an iodoform gauze pack is placed in the upper part of the wound. A No. 7 tracheal tube is inserted and a dressing is applied over the upper part of the neck.

Little reaction occurs following the procedure we have outlined. The temperature usually does not go above 100 or 101 degrees Fahrenheit for about 4 days and then comes down to normal. The drains are removed gradually; they are usually out about the tenth day. In a large percentage of cases, the closure about the posterior wall of the trachea and lower 5 centimeters of the incision almost heals by primary intention. A small pharyngeal fistula at the upper end of the incision is frequently freshened up after the wound heals sufficiently and is closed with mattress sutures. The tracheal tube is usually removed about the fourth day and kept out the greater part of the time unless there is some tendency for the tracheal opening to close. In this way less reaction occurs about the upper end of the trachea.

Age should not be a factor in determining the question of malignancy as we have had to perform laryngectomy in the case of a boy 16 years of age and in that of a man 77 years of age. While carcinoma of the larynx is less common among women, we have had to perform laryngectomy on a girl of 20 years. In regard to the question as to removal of lymph nodes in these cases, we do not do a routine block dissection of the neck of patients who have cancer of the larynx without glandular involvement. In cases in which there is glandular involvement of low grade we feel that this procedure should be followed.

A patient who underwent laryngectomy 18 years ago and who had palpable lymph nodes illustrates the value of block dissection in such cases. At the time of block dissection 2 lymph nodes were involved in the neck, and squamous cell epithelioma of grade 2 was diagnosed. The patient had no recurrence in the neck but died 15 years later of adenocarcinoma of the stomach. The gastric lesion had no relationship to the laryngeal growth. Patients with soft, rapidly growing metastatic lymph nodes are much better treated by irradiation whereas a patient who has hard, nodoty lymph nodes is better taken care of by block dissection followed by irradiation. Frequently however, one will be surprised by the results of block dissection and irradiation, even in cases in which tumors are of a high grade of malignancy. For example, a patient was operated upon and treated by irradiation for a carcinoma, grade 4, of the floor of the mouth, with metastasis to the cervical lymph nodes. The patient returned 10 years later in excellent general condition and with no recurrence which, of course is not the rule in such cases. We have not used the method of inserting radium into the growths following removal of the cartilage, as advocated by Ledoux, Harmer and Portmann. We feel that these cases are much better taken care of by surgical measures along with irradiation.

The results of treatment of carcinoma of the larynx have recently been reported by Yen and Waugh. In a consecutive series of 135 operations for carcinoma of the larynx, 75 thyrotomies and 60 laryngectomies, there was 1 death. In reviewing a series of 107 patients who were operated upon prior to 1929 they reported that 5 year cures were obtained in 81.3 per cent of the cases in which thyrotomy was performed and in 56.1 per cent in which laryngectomy was performed. It was found that the average time elapsing since operation in these cases was 9 years and 4 months, the shortest time being 5 years and the longest, 24 years. A review of the cases in which the growths had been graded microscopically showed that none of the patients with carcinoma of grade

4 was living 5 years later We are now treating such patients by giving them deep roentgen treatment, performing laryngectomy 1 month later, and following this again by deep roentgen treatment This, of course, makes a much more difficult procedure technically but apparently is producing better results We have 2 or 3 patients who are well now between 4 and 5 years after operation, and we anticipate that this type of treatment will produce better results than can be obtained by surgery alone We have recently seen a patient on whom Dr C H. Mayo performed laryngectomy 25 years ago, and this patient is perfectly well

In addition to the epithelial tumors of the larynx one occasionally sees an adenocarcinoma In this type of case the lesion may be removed surgically, following preliminary tracheotomy, in the same manner that one would remove a mixed tumor of the pharynx or parotid region

Sarcomas of the larynx are more unusual Figi recently reported 6 cases and New reported 2 These usually tend to be of a low grade of malignancy However, we do see those that are of the active fulminating type We have never seen a patient with an active type of epithelioma for which irradiation was used, where the patient stayed well over a period of years Some sarcomas, like one we recently treated, are pedunculated, this tumor filled the entire larynx and preliminary tracheotomy had to be done The tumor, which was attached only to the anterior portion of one vocal cord, was removed and the base destroyed by diathermy Microscopically it was a fibromyxosarcoma, of grade 4 There has been no recurrence in 1½ years, so that all highly malignant tumors apparently do not require radical removal if they are pedunculated

It is possible in the treatment of chondrosarcoma, to shell them out completely They vary in malignancy from those which are little more than chondromas, to very active malignant types Some of them extend well into the trachea and it is impossible to remove them in capsule One must rely in these cases on irradiation

Laryngopharyngeal tumors The postcricoid tumors are practically all squamous cell epitheliomas of grade 4, and in our experience, metastatic involvement of lymph nodes is usually present at the time of examination These lesions usually occur among women Trotter's method of taking care of them is the treatment of choice, however, the prognosis for these highly malignant tumors in this region is such that surgery offers little except in a limited group of cases We have seen these highly malignant tumors completely disappear under irradiation but the patients stay well for only a little more than a year

We recently operated on a patient with a postcricoid tumor, squamous cell epithelioma grade 3, somewhat pedunculated, that was attached to the posterior wall of the pharynx and upper part of the esophagus Following tracheotomy, we performed transthyroid pharyngotomy and were able to remove the tumor by means of surgical diathermy The patient was well and without recurrence 1½ years later

In some cases in which the growth is fixed to the posterior surface of the larynx, without involvement of the rest of the upper part of the esophagus and without any lateral extension, it is possible to perform laryngectomy and save the upper part of the esophagus In this way closure may be made without requiring a flap of skin, as in the Trotter operation

Tumors of the pyriform fossa are usually of a high grade malignancy and, like postcricoid tumors, usually metastasize early In general, irradiation offers more than surgery, as these growths usually do not produce symptoms early enough to bring the patient for examination when surgical measures are worth while

CONCLUSIONS

In the treatment of all malignant lesions of the larynx, it is essential that the individual case be carefully studied and that no definite technical procedure be fitted to the case until the larynx is explored, and the best method of completely removing the diseased tissue ascertained The method chosen should leave the patient with a good voice when it is at all possible

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THE DIAGNOSTIC CANCER CLINIC IN A PRIVATE HOSPITAL[1]

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IN 1900 cancer stood sixth as the cause of death in the United States. At the present time deaths from cancer stand second only to heart disease in total mortality rates.

With the beginning of the present century extensive research and experimentation advanced so rapidly that it is now impossible for any individual to be a master of all branches of medicine. Specialists have appeared and special groups for the diagnosis and treatment of various maladies, including tuberculosis, venereal disease, diabetes, etc. It is a well known fact that cancer may attack any part of the body and be characterized by various types of tumors. The patients in clinics and in charity hospitals have had the advantage of being studied by specialist groups. Private patients, however, were not always so privileged. In 1928 therefore the malignancy committee of the Hollywood Hospital was formed to try to bring the benefit of group opinion to the private patients.

One of the first requisites in the management of a malignancy case is diagnosis. Due to inadequate facilities for training, or because of the sparsity of cases, the number of cancers seen by the average physician and surgeon each year is usually not over 5; therefore, physicians and surgeons individually have little opportunity to become proficient in the diagnosis of malignancies in the early stages.

It has been well pointed out by previous writers on the subject that the avoidable delay elapsing from the time the patient first notices his or her tumor to the time of seeking medical advice is 4 months. It has also been pointed out that the avoidable delay after the first examination by the physician to the time that the patient receives proper and efficient treatment, is 3½ months, so that the total avoidable delay time throughout our country averages 7½ months before correct treatment is instituted. The taking of biopsies is feared by many physicians and many are not equipped to make them. Physicians as a whole seem somewhat hazy in their opinions as to proper forms of treatment in certain given malignancies. Group examination and opinion is therefore more quickly sought by the physician for his patient if these groups or clinics are available for use. The patient is usually much impressed by a group examination, is also more willing to accept the situation as it is found and will therefore not wander from one physician to another seeking further advice.

Treatment must be not only prompt but adequate. A little treatment because a lesion may be cancer is unjustifiable. The original treatment must be carefully planned and then meticulously followed. Secondary treatment after failure of the primary is rarely successful.

There is no doubt as to the benefits of group opinion in malignancy; our problem has been to apply this method in a private hospital.

The malignancy committee of the Hollywood Hospital began to function in 1928 and has continued to the present time. Meetings are held once each week. The personnel of the committee has changed very little since its inception, being composed of 5 members: a general surgeon, a gynecologist, an internist, a pathologist, and a radiologist. The committee elects its own chairman, vice-chairman, and secretary annually. The record nurse and malignancy interne are appointed by the hospital, as is also a consulting staff consisting of a proctologist, oculist, aurist, dermatologist, urologist, and plastic surgeon. The consultants are not required to attend the regular weekly meetings, but are required to examine patients referred to them, and report their findings in person or in writing at the next meeting.

The routine procedure of the committee is as follows: Patients are referred to the malignancy committee by any regular physician by card or letter. A history is taken on the regular malignancy form by the malignancy interne and this history is read in the committee room while the patient is being prepared by a nurse in the examining room. After the patient is examined, the case is immediately discussed in the committee room. Special laboratory work, X-rays, or special examinations, if needed, are requested of the referring physician. But, as a rule, he will direct that such work be done at the hospital. Biopsies are taken, with the consent of the referring physician, by one member of the committee and the findings are reported by the committee pathologist.

After full discussion of the case examined and completion of a diagnosis, the committee then jointly arrives at the most appropriate treatment. This method lends definite individuality to both diagnosis and treatment of each case. The chairman then dictates a letter to the referring physi-

[1] Presented in the Cancer Symposium, before the Clinical Congress of the American College of Surgeons, San Francisco, October 28–November [illegible], 1931.

TABLE I.—STATISTICS OF MALIGNANCY COMMITTEE, HOLLYWOOD HOSPITAL, JANUARY 1, 1929—JULY 1, 1935

Year	New cases	Patient visits
1929	108	157
1930	110	193
1931	127	236
1932	162	401
1933	225	530
1934	237	459
1935—to July 1st	108	173
Total	1077	2149

TABLE II

	Number
Patients referred by doctors on Hollywood Hospital staff	809
Patients referred by other doctors	182
Patients not referred by any doctor	86
Cases referred by 251 physicians	991
Physicians referring from 10 to 45 cases each	23
Committee meetings from January 1, 1929 to July 1, 1935	332
Hours consumed in meetings	750
Letters written to physicians	1115
X-ray pictures taken of breast cases for diagnosis	400
Papers on cancer read outside hospital	15
Papers on cancer read before Hollywood Hospital staff	20
Cancer clinics held before Hollywood Hospital staff	4
Annual meetings of the American College of Surgeons attended by delegates	4
Annual meetings of California State Medical Society attended by delegates	3

cian and the patient is directed to call on his or her physician in 2 days No information whatever is given to the patient either verbally or in writing Letters to physicians are descriptive of the lesion found with definite attempts being made to give a concrete diagnosis, with the committee's suggestion as to treatment of the case

Records on all cases are kept on file, with a follow-up These records are available for statistics and reference work both by the committee and the patient's physician In cases entering the hospital after examination by the malignancy committee, a copy of the consultation letter is attached to the history on admission Following any operation or treatment given, case copies are transmitted from the hospital record office to the malignancy file of this patient This includes all pathological, X-ray, and operative reports

Treatment of patients is undertaken by members of the committee only on the written request of the physician referring the case

When the committee has had an unusually difficult case all the data is collected, including laboratory slides, X-ray films, etc, and these, with descriptive letters, are sent to cancer centers elsewhere, for advice The staff of the Memorial

TABLE III —COMPILATION OF TOTAL CASES FROM JANUARY 1, 1928—JULY 1, 1935

Type of case	Total number	Malignant	Non Malignant
Breast	292	124	168
Cervix	134	63	71
Uterus	70	19	51
Vagina	11	2	9
Vulva	7	3	4
Pelvis	32	15	17
Rectum	40	28	12
Colon	9	6	3
Stomach	16	11	5
Esophagus	3	2	
Liver	6	5	1
Lung	7	3	4
Mediastinum	4	4	0
Pancreas	5	5	0
Genito urinary	26	11	15
Bone	18	9	9
Skin	32	12	20
Hemangioma	13	0	13

TABLE IV

Type of case	Total number	Malignant	Non Malignant
Ear	9	6	3
Eyelid	12	7	5
Face	80	53	27
Jaw	8	6	2
Lip	59	27	32
Nose	50	19	31
Mouth	29	11	18
Throat	12	8	4
Tongue	49	15	34
Scalp	5	2	3
Neck	28	16	12
Parotid	5	3	2
Branchial Cleft	1	1	0
Thyroid	3	0	3
Melanosis	3	3	0
Carcinomatosis	4	4	0
Sarcomatosis	6	6	0
Miscellaneous	84	9	75
Total	1172	518	654

Hospital in New York has been most generous in assisting our committee in these complex cases By using air mail we are enabled to receive a reply from this hospital in 1 week This aid has been much appreciated, and we wish to express our thanks to the staff of the Memorial Hospital for their generous advice

We do not feel that the formation of cancer committees or tumor clinics in hospitals produces cancer phobias, no more so than does the publicity given tuberculosis and various other diseases We do feel that a cancer clinic is of great importance to physicians of the community and to the internes of the hospital Physicians referring patients, or visiting the clinic meetings, of necessity are better able to recognize early cancer and will continue to become more cancer minded in their daily routine

Reference of suspected malignancy cases to the malignancy committee is purely voluntary on the part of the staff. Some staff doctors are self sufficient and do not wish advice others are fearful that asking or taking advice will belittle them in the eyes of the patient or that they might lose their patient. On the whole the response of the Hollywood Hospital staff has been more than satisfactory as shown by the number of patients referred. Twenty per cent of the total number of patients examined thus far have been referred by physicians not on the Hollywood Hospital staff These outside physicians are also frequent visitors at the regular meetings.

The economics of a diagnostic cancer clinic in a private hospital may be summed up briefly as follows

No financial burden should be placed on the hospital *per se* The physicians forming the committee are without compensation, and any routine biopsies or minor laboratory procedures are referred to the pathological laboratory and reported without charge, as also are small X-ray films. Three rooms are placed at the disposal of the committee by the hospital, together with nurse and recording secretary without charge.

Patients referred to the committee on their first visit are handed a slip of paper upon which is written a statement in two paragraphs, telling the functions of the committee and asking for donations to defray necessary expenses, including printing stenography histories, etc. These donations have varied from twenty five cents to one thousand dollars.

There are certain physicians who, after a diagnosis of malignancy is made on their patient, refer the patient back to the committee for recommended treatment. These patients, if hospitalized are treated as committee cases and an appropriate fee is charged to cover all necessary hospital expenses. Any remaining fee is credited to the malignancy committee fund Gratuitous services rendered, as stated, have apparently repaid the hospital many times, in that a large majority of these patients have been hospitalized in the Hollywood Hospital for the treatment suggested by the malignancy committee Therefore the administrative departments of private hospitals should assume a very optimistic attitude with regard to recompensation for gratuitous services given by their full time pathological, X ray or nursing departments

The malignancy committee fund is used in the purchase of essential stationery films, photographic apparatus, and there have always been funds available sufficient to repay expenses of one member to the annual meeting of the American College of Surgeons This member in turn is expected to spend the majority of his time at the convention in cancer work and it is his obligation, on his return to present to the committee and other interested physicians, a formal report of knowledge gained.

SUMMARY

The malignancy committee of the Hollywood Hospital believes that.

1 The diagnosis and treatment of cancer is a specialized subject and not one in which the majority of the physicians and surgeons have the opportunity to become proficient.

2 The diagnosis and advice as to treatment by a group of cancer minded physicians acting in unison, with adequate diagnostic facilities, make for efficiency in protecting the interests of both the patient and the patient's physician.

3. The avoidable delay time before proper treatment is instituted, which is now approximately 7½ months, must be cut down appreciably before our results will show improvement

4. Accurate diagnosis by biopsy if possible should be made before treatment is instituted and that treatment must be prompt and adequate—a little treatment because of a little doubt in the diagnosis is unjustifiable

5. The life of the cancer patient depends on the first physician who sees and treats him secondary treatment after failure of the primary treatment is rarely successful

6. The diagnostic cancer clinic is practical and workable in an accredited private hospital so long as the rules and ethics of medicine are followed.

The accompanying tables give statistics covering the work of our committee

SYMPOSIUM: TREATMENT OF FRACTURES

THE CAUSES OF NON-UNION BONE GROWTH AND REGENERATION[1]

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PHILOSOPHY constantly seeks new fields for investigation It is, without question, the driving force of the universe, always turning, twisting, and struggling in an effort to go forward, to make things more perfect and to discover new and imperfect things that it may perfect In other words, philosophy is insatiable and we must endeavor to support any study or investigation that will increase our knowledge and make surgery and medicine more exact sciences But the efforts to perfect our knowledge must not be allowed to obstruct our use of those facts which we know to be true This paper is an effort to correlate the known facts about bone growth and place them in a workable formula

When an investigation of this subject is undertaken, one is confronted with an almost unbelievable chaos, brought about by the confusion of terms and the multiplicity of conclusions, in many instances the conclusions being drawn from insufficient data

While it is acknowledged by most physiologists that bone can and does grow, the great argument in their minds is what makes it grow and from which of its 3 major components is the greatest growth obtained There is no doubt whatever, either in the mind of the physiologist or of the surgeon, that, when the shafts of 2 fragments have been denuded of periosteum and are approximated, the cortical bone or osteogenic layer rapidly produces bone and a very firm union takes place And the firmness varies with the area of approximation "Femurs of heavy men with 2½ inches overlapping are firmly united in 6 to 8 weeks " Hence the statement is still present in so many textbooks as to the length of time required for femoral union

But, when 2 fractured femoral fragments are approximated, one covered with periosteum and the other denuded of periosteum, another problem is presented, in that the union depends entirely upon the ability of the denuded bone cortex to produce a shelf upon which the other fragment may rest, while the intervening periosteum is absorbed or destroyed Or, if the non-denuded sides of both fragments are approximated after the force has ceased and the treatment has been instituted, a non-union is the common result. The open ends of this fracture will absorb bone fragments, produce some bone, and seal the ends, but there will be no union

In these types, which every surgeon encounters at different times, there are certain very definite facts that make themselves evident The first is that cortical bone will grow and grow rapidly The next is that the periosteum can and does block efforts at union when the conditions are not favorable These facts do not mean that the bone will always grow or that the periosteum will always inhibit growth The bone growth from the ends of the fragments is always slow, because at the point of fracture there is always a layer of so called dead bone and this must be mobilized and utilized before a union can take place In the ends of femoral fragments, these being the largest bones, we find the greatest amount of so called dead bone Or to put it in what our clinic thinks to be the best description, the layers, or borders, or edges of bone fragments are devitalized to the extent that bone cells in the lacuna will not take the hematoxylin stain And these ends and the fragments are without doubt in a resting stage, but are not dead in the sense that a piece of boiled bone is dead We are firmly convinced that this dormant bone is present to a greater degree in the femur than in any other bone, because of the fact that for many millions of years femoral ends were seldom, if ever, approximated, and the accustomed manner of healing has been by an overlapping and cortical contact We are convinced that the end-to-end reduction of transverse fractures of the femur by traction and manipulation requires from 30 to 50 days longer to obtain a firm union than any other type of femoral fracture This delay, which is caused by the readjustment of the so called necrotic or dead end, or, as we prefer, the dormant end, excites many surgeons to examinations and manipula-

[1]Presented in a Symposium on Fractures before the Clinical Congress of the American College of Surgeons San Francisco, October 8–November 1 1935

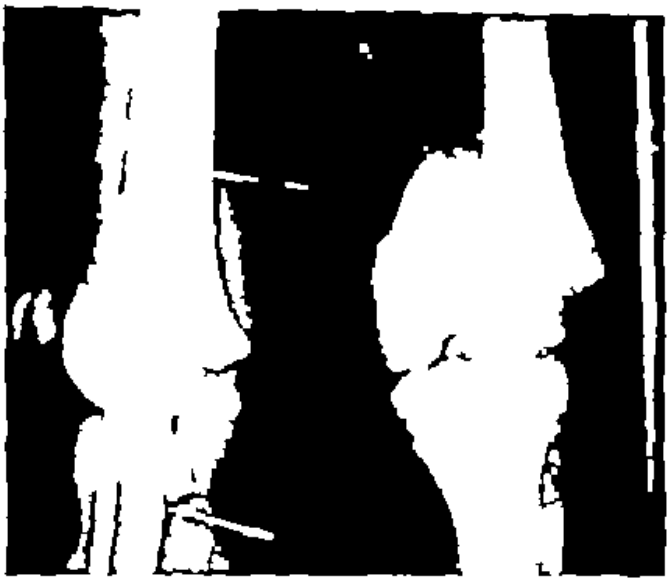

Fig J J C Marked development of detached periosteum in an adolescent. The epiphyseal lines are still visible The periosteal bone is more dense than the bone adjacent to the shafts

tions that may destroy the new callus and cause a non-union We do not mean to infer by any means that a crack or breaking of the callus will always cause a non-union, because such is not the case But repeated manipulations and multiple readjustments are certainly a factor in the production of non-union *Surgeons should realize* that many transverse or slightly oblique fractures of a femur require from 90 to 120 days for firm union, if the ends are correctly approximated. Possibly if the traction could be so adjusted that the tone of the muscles could make normal pressure without permitting a bowing of the bone a firmer and more rapid union might take place

The speed of bone proliferation and the firmness of union in oblique fractures, in which there is no interposition of tissues, causes us to wonder if there is a layer of devitalized bone in this fracture parallel with the *haversian canals, of equal* depth to that on the ends of transverse fractures We could not find articles of proof either in *animal experiments or in observations* upon the human

That injuries may be so terrific that the periosteum may be torn into many ragged fragments or torn from the bone as a whole, leaving one fragment completely denuded, there can be no doubt, as we have observed both types That there are any number and types of variations must be admitted as possibilities Now, if one fragment is torn out of its periosteum and the periosteal tube twisted to cover the non-denuded end a non-union is almost certain to result. On the other hand if one torn flap of periosteum and attached fascia and muscle is placed between the bone ends, *it will tend to inhibit and delay* bony union, because as far as we can determine from the literature and observations, only one side of the periosteum will produce bone.

So much for the periosteum as an inhibitor of bone growth. It should be stated, however that the picture produced by strips of periosteum elevated from each fragment and the luxuriant growth of callus between it and the fragments, convinces most observers that when conditions are favorable periosteum is of the greatest aid in callus formation We, however have never observed a detached strip of periosteum in an elderly *individual growing bone at a distance from the* fractured bone whether it was or was not attached at one end. The reader must be careful not to get this finding confused with the wild growth of bone so commonly seen around the elbow as that apparently is from an unknown and very different cause.

In young people, periosteum detached from the shelf adjacent to each bone fragment will, not uncommonly show a growth of bone immediately attached to the periosteum with a relatively smaller and less dense amount of bone in the area adjacent to the cortex (Fig 1) This very *rarely occurs in the adult* As *just stated*, however a strip of periosteum adherent at one end with the other end widely displaced from the fracture has never in our experience shown a growth of bone at its distal portion

Another factor that must be considered is injury to the blood supply of the bone with the periosteum intact or with an avulsion of the periosteum So far as we have been able to observe interference with the blood supply alone causes little disturbance This means that under ordinary circumstances, fractures at or near the nutrient artery heal just as well as those distal or *proximal to it But when the fractured end*, distal or proximal to the nutrient vessel which has been injured is also denuded it is common to have non-union and at the time of operation the surgeon will expose one of the fractured ends of the bone which will be white with a slightly pink color showing through the white, the edges rounded and the loose fragments absorbed, but no evidence of any effort at bone proliferation from this fragment The bone is alive but dormant, and a slow union may be prognosticated, *irrespective of* the method used in the repair It is well to state here that a bone fragment that is well nourished is of a rich, dark red color with blood oozing freely

from multiple small points These pale fractured ends which we have designated as dormant are most commonly of an oblique or spiral type, but we have encountered one transverse fracture in which three-fourths of the cortical area presented the findings described It is well known that the condition described in the dormant ends is commonly found in detached fragments, but we wish to emphasize strongly that this condition also occurs in the fractured end or ends of bone which have had their vitality interfered with by an injury to the blood supply and an avulsion of the periosteum In this type of dormant bone, the cells may or may not take a normal hematoxylin stain We have not observed a sufficient number of cases to be certain, and in those observed we have had difficulties with our specimens which we hope to overcome Good roentgenological studies will show that the dormant fragments are much more dense than the normal fragments

Non-union following an early open operation with steel plates, ivory or boiled bone plates, onlay or intramedullary grafts of autogenous bone in many instances will be traced to this dormant condition of one of the fragments This dormant condition can be present as a result of the accident itself or as a result of the ruthless sacrifice of the periosteum at the time of operation However, if this condition is encountered in non-union and there is also some interposition and an exuberant callus from the other fragment, the new callus when approximated to this bone, seems to adhere quickly to the dormant bone and, we think, stimulates it to growth

We are convinced that there is less dormant bone on the ends of a transverse fracture of the humerus than on the ends of femoral fractures and that these ends will grow new bone much more rapidly than any other bones in the body, possibly because in our millions of years in the upright position they have been much more frequently brought end-to end where the broken fragments have been brought into apposition or slightly separated by the weight of the pendant distal portion of the upper extremity

In explaining why cartilage is a common accompaniment of bone growth do not forget that as life evolves bone is far more recent than cartilage and has been developed by the organism when a more rigid supporting structure is necessary The beginning of bone is a calcium deposit in cartilage, later a bone structure becomes organized in the calcium deposit These same steps are found in the healing of different types of fractures the process varying with the blood supply In our opinion these steps have no clinical significance

Up to the present time we have dealt with non-union from an anatomical standpoint but we are now ready to present something upon which to prognosticate a non-union at the time the patient is brought into the hospital While as a rule, the history, as far as it concerns the production of a fracture and as related by the individual has little value, the history obtained from the patient and from other observers should be of great value It must be determined how long the force that produced the fracture continued to act, for it is the continuation of the force that has caused the interposition of tissues, that injures and destroys the periosteum, that causes its twisting and being torn to bits, as well as injures the blood supply of the bone and the adjacent tissues It is a simple thing for an individual to crack a leg or an arm, have it immediately put to rest, and obtain a union But if that arm is caught in a belt and jerked around a pulley many times with its possessor following after it, a union is far less likely to occur To use another example, suppose there is an automobile accident The thigh of one of the car occupants is fractured at the moment of impact the automobile turns over two or three times and in the end, the individual is thrown out During these movements he is shaken around in the car like a pea in a pod and obviously the limb is twisted into every possible angle during that shaking up These are examples of what is meant by the continuation of the force following the reception of a fracture These factors are the common causes of interposition and devitalization of bone fragments and these, in our opinion, are the commonest causes of non-union

Messy manipulation and frequent interferences in the treatment are other vital factors These manipulations and interferences with the growth of the callus are frequently stimulated by the fact that the X-rays fail to show the growth of callus We have repeatedly observed firm union in which no callus was visible in the X-ray plates We wish to caution the reader not to place too much stress upon the X-ray evidence as to the absence of callus We have operated repeatedly with the idea that there was little, if any, callus present and have found a well developed callus We have examined patients in whom callus was reported absent in the X-ray film and yet we have found union present If in doubt, wait and do the least possible amount of handling and manipulation

We have observed other cases particularly in the upper 4 inches of the tibia in which the force was not great enough to cause displacement of fragments and an interposition of tissues, or to interfere seriously with the blood supply, and yet

Fig. 2. M T. 8 years of age. Congenital non-union of both bones of the left leg. At 8 years of age grafts were taken from the right tibia, which is shown in this illustration, and the site from which the graft was removed has regenerated new bone and some excess bony growth. This is to be expected in all children. At a subsequent operation, a small piece was taken off of the proximal fragment of the ununited tibia. In this abnormal bone there has been no effort whatever at regeneration, either at the spot where the graft was removed or where there should be union. Like the grafts, yet the grafts from the right limb have lived and increased in size with the growth of the individual.

Fig. 3. J F. 8½ years of age. The defect in the tibial crest, anterior and lateral views, 4½ months following removal. No effort at regeneration.

there has been non-union, due to the fact that the bone just did not grow. It is the one place in which a fracture has occurred and we have been able to be certain that there was no interposition, yet a non-union has resulted. Without manipulations or any other factor we were cognizant that there might result a non-union.

Multiple fractures as a cause of non-union are well known but we believe that these fractures do not unite because of a continuation of the force and interposition, rather than because of the multiplicity of bone injuries.

Most of our repair of non-union and malunion has been accomplished with onlays and intramedullary grafts. We have not been particular about the preservation of the periosteum on the graft but we have been very particular about the periosteum on the fragments where there was to be an onlay or intramedullary graft, removing only as much periosteum as was necessary to make a bed where the onlay was to be applied and not removing the periosteum from bones where the medulla was to be injured by an intramedullary transplant. However in the future, where we use onlay grafts we shall preserve the periosteum because without question, the connective tissue and periosteum when transplanted do not die. Evidence is accumulating that the fragment will receive an earlier and better blood supply if the periosteum is allowed to remain intact. We have used detached strips of periosteum in an effort to aid the proliferation of bone in cases of non-union, where we have used an autogenous bone graft, but as yet we have never seen it show any evidence of bone proliferation or thought that it aided bone proliferation in any manner.

The intramedullary grafts are all autogenous, roughly triangular in shape, and seldom, if ever fixed firmly in the canal. We are sure that they do better if they are firm rather than loose but we have fear of a necrosis of the cortex if they are driven in too tightly. However we can say that we have seen no cortical necrosis if the periosteum has been left intact, even if the graft has been firmly driven into the medullary canal.

In relation to the life or death of these transplanted fragments, it is definitely known that all of the adult bone cells are dead, shrunken, and shriveled, as is shown by the hematoxylin stain. But we are firmly convinced that there is life in a transplanted fragment, and it remains for our in-

Fig 4 M P , 29 years of age Defect in the tibial crest from which fragment had been removed 18 months previously No effort at regeneration

Fig 5 T M , 65 years of age Tibia from which grafts were removed 5 years previously Shaft is thinned and narrowed No regeneration

vestigators to devise some manner by which this life can be demonstrated microscopically These fragments retain their same shape, they become pale with a little pink showing through, and later on they become firmly adherent to the adjacent bone and other structures At a later period when the structures adjacent to them are removed, they will bleed and at the same period, if fractured, they will reproduce bone As Ryerson says, "If, like the autogenous graft, I can retain my same shape, feed, and reproduce, death will have no sting "

If these autogenous fragments are boiled for one or more minutes, none of the phenomena mentioned will be observed, it is a true sequestrum and will remain such, it will absorb fluids and after several weeks or months will cast a very faint shadow as compared with the shadow cast by normal bone It is frequently firmly adherent to the surrounding structures and seems to be less irritating than a metal fragment, but it never grows, never bleeds, and never reproduces bone Absorption of boiled bone has been observed experimentally and does occur in the human animal, but it is not common and cannot be prognosticated As to which cell is osteogenic and which is not, we have no brief but we are firmly convinced that the cells between the cortex and the periosteum are the most vital factors in the reproduction of bone Whether these cells are derived from the inner layer of the periosteum or from the cortical bone, we do not know Nature is obviously cognizant that the adult bone cell in its lacuna is useless and so permits it to die But no one has been able to observe the activity of one of these bone cells freed from its lacuna

Now to discuss the area from which autogenous bone grafts have been taken A number of radiologists and orthopedic surgeons with whom I have spoken are positive that this area will fill with normal bone at an early date Most of these men, however, have been judging this bone replacement as it occurs in young people We also have seen the bone replaced in young persons Figure 2 shows the right tibia from which multiple grafts have been removed, and yet this bone has refilled the spaces from which the fragments have been taken and has added an excess of bone In the

Fig. 6. J.H., 55 years of age. Rectangular area removed from flat surface of tibia to repair lateral condyle. Very slight regeneration.

other leg, where the graft has been planted, it can be seen that the graft has grown but along with its increase in size it has retained its same shape although it has not formed a union with either the upper or lower fragment. In the edge of this tibia to which the graft has been applied may be seen an area from which a fragment has been removed, and at the end of 5 years that fragment has not been replaced the defect remains the same. This child was 8 years of age when the fragment was removed. The last picture, which still shows the defect, was taken when she was 15. The normal bone has refilled its space and the congenital non-union is running true to form and has not produced bone.

Figure 3 was taken 4½ months after a bone graft had been taken from the upper end of a tibia. The patient was a boy 18 years of age. The edges have been smoothed off and yet no effort at bone reproduction has been made. This is the youngest individual we have had who has failed to reproduce and refill a bone defect.

In no adult have we observed the regeneration of the anterior tibial border from which a fragment of bone has been removed (Figs. 4 and 5). Where the anterior surface of the tibia has been removed in order to obtain a transplant and the medulla has been uncovered, we find that a very thin layer of bone has regenerated. This layer is so delicate in the middle of the defect that an artery forceps can be pushed through it. It is a little heavier around the edges but it never reaches anything approaching the full depth of the original cortex (Fig. 6). The edges of these areas are all smoothed off and the detached fragments absorbed, but no bone growth occurs to obliterate the space. It has made no difference whether these fragments were removed with a saw in which case heat might have been a factor or with a chisel where no such lethal factor could be considered. We have had fractures occur in 2 of these cases from which fragments have been removed for grafts. Strange to say they entered the ward within a week of each another they were the first cases of the kind we had ever seen, and, though a year has elapsed since they entered the ward, we have observed no other since.

We have considered carefully the articles in the literature on phosphates and are sure that it is the factor in the growth of young bone. We think that some day it may be utilized to activate the growth in adult bone and to aid in healing. The use of calcium salts in the production of a union, given orally intravenously or injected at the site of the fracture, has not proved to have the least possible value. My associates are convinced that the use of a certain vitamin product, the name of which I do not wish to mention, had a distinct influence upon the production of arteriosclerosis, but the evidence is too uncertain to justify a positive statement. Further investigations will be conducted.

The treatment of non-union by boring holes back and forth through the un-united area receives considerable comment in the literature one article reporting 19 cases with 19 cures. We believe that this method will be successful in probably 40 per cent of the cases, and then it can be successful only if there is a very close approximation of the fragments and a very small amount of interposition.

CONCLUSIONS

On bone growth the following facts are evident:

1. We believe there is life present in autogenous bone grafts as evidenced by retention of its form, subsequent bleeding and later the reproduction of bone if fractured. This life cannot be demonstrated by the ordinary histological methods but, in our opinion, it will be demonstrated later by new histological methods.

2 Boiled bone, whether autogenous, homogenous, or heterogenous, always remains a sequestrum Under certain unknown conditions it may be absorbed

3 Periosteum can and does develop bone, but it can also, under certain conditions, interfere with bone growth

4 In the adult, bone defects of the tibial border removed for transplant will not be regenerated Where the cortex has been removed, bone defects are regenerated in a very imperfect manner, many times no regeneration at all occurring

Non-union most frequently results from the following causes

1 Excessive force that continues after the fracture has occurred, producing injury to the periosteum, the structures adjacent to the bone, and the blood supply of the bone

2 Messy manipulation carried out with the hope of ascertaining whether there is or is not a union

3 Failure of bone to regenerate in certain fractures of the upper end of the tibia with no chance of interposition

4 Other factors, almost too numerous to mention, have been given as causes of non-union but, in our experience, have had little, if any, significance

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THE STATUS OF FRACTURE TREATMENT IN THE FIELD OF SURGERY[1]

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THE treatment of fractures has advanced by tremendous strides in the last two decades It has had to do so, first, to cope with the problems arising in and from the Great War, and then to deal with the situation created by the placing of fracture treatment on an economic basis as the result of Workmen's Compensation legislation It is rather interesting that the astonishing improvement which has taken place has not resulted in the enunciation of a single new principle, but has been the outcome of forced recognition of the significance and implications along pathological and physiological lines of basic principles evolved many years ago As a natural consequence of this new conception of the meaning of basic principles, there have been developed methods of treatment calculated best to meet the new demand, that of not only making the injured man well, but of doing it in the shortest possible time and at a minimal cost.

When fracture treatment was pushed into the economic field, a new importance was given the subject. Once regarded as the orphan child of surgery, it has now become an object of solicitude Foster parents clamor for its custody Today the status of fracture treatment in the field of surgery might well be described by the popular witticism: "All dressed up and no place to go"

The orthopedist is firmly convinced that in him lie the qualities which make for proper guardianship of this heretofore neglected child of surgery The general surgeon is just as certain that the proper bringing up of the little one is *his* sacred duty And, as is often the case in matters of dispute, they are both wrong It is time that a few plain truths are recognized before the child dies of too much misdirected solicitude

In the first place it is to be kept in mind that the care of the vast majority of fractures will never be in the hands of either surgeon or orthopedist In the second place, it is a debatable point as to whether the ability to care for static, mechanical, skeletal defects and disease of the skeletal system carries any greater implication of capability in the treatment of fractures than does the ability to treat the interior of the abdomen adequately Both fields come under the heading of surgery So does fracture treatment But the principles involved in the treatment of fractures are just as different from those involved in the care of bone and joint disease as they are from those involved in the care of gall-bladder disease.

Injury has a pathology all its own It has physiological repercussions peculiar to that pathology And the adequate care of injury is based on principles founded on adequate understanding of that pathology and its physiological implications To treat fractures with economic efficiency by present day methods requires that the doctor be a surgeon, that he be an orthopedist, but that he have, in addition, appreciation of the peculiar pathology and pathological physiology that char-

[1]Presented in a Symposium on Fractures before the Clinical Congress of the American College of Surgeons, San Francisco, October 28–November 1 1935

acterizes injury as opposed to disease and to deformity

What, specifically does all this generalization mean? It means that efficiency in fracture treatment demands specialized knowledge and training not denoted by the label "orthopedist" or "general surgeon. It constitutes a field in itself. The term "Traumatic Surgery" has been applied to this field. That the appellation "traumatic" has an ironic justification is due to the fact that the care of injury in the average medical school and hospital is considered merely incidental to either the surgical or the orthopedic service.

What must be done then, that this bewildered child of surgery may find itself?

First, recognize the fact that the general practitioner must handle the majority of fractures. Teach him in medical school and hospital how to handle adequately those which he is capable of handling, and how to recognize those which are beyond his capabilities when he first sees them, not after he has proved his insufficiency These latter are the cases which require a special knowledge and training for their adequate care and they all too often get the advantage of it only *after* the results of the lack of it have been thoroughly demonstrated

Second, recognize that the field of fracture treatment as a special one, requires peculiar knowledge and training in the post-graduate education of interns, residents, and junior staff members. This of necessity means centralization and segregation of cases of injury in hospital wards it means adequate organization May I stress that word—"organization." It is of much more importance than the doctor in the care of injury I say that advisedly Modern treatment methods make proper organization absolutely essential to success. The best man in the field can get but indifferent results without it. A distinctly average man can get excellent results with the proper organization, if he but understand the principles involved. Economic pressure today demands adequate care of the injured Time and money are the criteria by which results are evaluated, just as much as appearance and function The treatment of a certain number of fractures constitutes a special field requires specialized training and demands, for success, adequate organization not only in the medical school but in the hospital.

The child doesn t need a guardian or a home It has grown up and it is building its own place and must continue to do so.

THE TREATMENT OF 278 CONSECUTIVE FRACTURES OF THE FEMUR[1]

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THE treatment of fracture of the femur involves the study of a very important and useful member of the human body These fractures occur in individuals of all periods and vocations of life The femur constitutes an integral part of the lower extremity and is designed to bear the weight of the body and to serve as a means of locomotion Its lateral position, in relationship to the pelvic girdle and spinal vertebræ, necessitates its development as a complex mechanical structure, which is perfectly balanced under normal conditions to perform its specific functions

The human body normally occupies one of three positions standing, sitting, or lying These positions are maintained under normal conditions by a proper balance between the lower extremities, pelvic girdle, and spinal column This balance may be disturbed both anteroposteriorly and laterally

Any solution of continuity of the femur, which causes a deviation of the normal alinement or produces any disturbance of the normal relation of the extremities to the trunk, interferes with the function of support, locomotion, and proper balance, and also casts its reflexion upon the function of the spinal cord, chest, abdominal and pelvic viscera The underlying principles in the treatment of such fractures, should be the restoration of function and equilibrium of the limb when balance has been disturbed

A careful review and analysis of our own work over a period of many years brings to light the many difficulties encountered in the early days and the institution of better and more modern methods within recent years

The increasing demand of industry and the intelligent public for better results should keep us mindful of our duty to a problem which we should consider as within the realm of major surgery, but which until within the past few years, has been looked upon lightly by the general surgeon

Space does not permit a broad discussion of the problem, so that we hope that merely a brief statement of our own experience in the development and progress of our work on fracture of the femur from 1916 to 1935 may be helpful Throughout this period, we have striven constantly for a more constructive standard of treatment A careful review of the early literature reveals a high incidence of disability and mortality, a fair proportion of which was directly traceable to the lack of proper first aid, to improper medical service, and to poor transportation facilities

A great proportion of our series consists of an industrial group of patients, employed in the mines of the Pittsburgh Coal Company, whose activities lay within a short distance from Mercy Hospital, Pittsburgh, Pennsylvania An organized plan by the employer to improve conditions has occasioned the training of 80 per cent of their employees, who now hold first aid training certificates First aid stations to the number of 173 have been installed within 21 mines Each station has complete first aid equipment The physician s emergency office is conveniently located at the entrance to the mine The patient is immediately rendered service by his companions with prescribed first aid methods The strict routine of these methods, when properly instituted, so that the patient may be transported safely to the hospital, reduces the dangers of further destruction of tissue and the development of shock, as has been pointed out in timely fashion by Bancroft

We have always entertained a feeling that the story of success or failure in the treatment of fracture of the femur, whether it pertains to restoration of function or mortality, is written during the first 48 or 72 hours after injury

Our preliminary measures are quite conservative and cautious An immediate survey of the patient is made to reveal the presence or absence of shock, the type and nature of fracture, and the character of his associated injuries If only moderate shock exists, and the first aid immobilizing splints are secure, he is carefully placed in bed without the removal of his clothing, to minimize further trauma, to avoid further shock and to escape the infrequent but occasional sudden death from fat embolism Preliminary X-ray films as a rule are portable When the condition of the patient permits, the limb is carefully cleansed, shaved, and temporarily immobilized by a Buck's extension and is retained in a Thomas splint Further measures for the control of shock are

[1]Presented in the Symposium on Fractures before the Clinical Congress of the American College of Surgeons, San Francisco October 28–November 1, 1935

instituted; if already present, immediate therapy is established for the prevention of impending intestinal ileus. The frequent occurrence of intestinal ileus has inspired us to anticipate its development and to establish prophylactic treatment. Its insidious onset and progress frequently prove confusing to the inexperienced physician. It is difficult to control and is extremely tragic if permitted to develop to its full state.

Reduction of simple fracture of the femur of all types by the time honored Buck's extension method, protected by coaptation pads, and supported by the Thomas splint, has proved successful in about 10 per cent of our cases. Its application has been quite useful in the aged and young children and in certain badly comminuted fractures of the shaft. Successful reduction of displaced fractures of the shaft by this method alone has been rare. We have been quite cautious in attempting reduction by manual traction and manipulation. The use of local anesthesia about the site of fracture reduces the degree of activity and lessens the danger of fat embolism and further tissue injury. This method with the aid of the fluoroscope, has proved quite useful in the hands of Campbell and others. The method described by Russell in 1924 with Mahorner's recent modification is undoubtedly safe and worthy of much consideration.

The advent of direct skeletal traction offers definite advantages. The Kirschner wire and Steinmann pin, which have supplanted the use of the ice tongs, have been very satisfactory. We have confined their use chiefly to the supracondyloid and comminuted displaced fracture of the lower third of the femur. The insertion of the wire or pins through the supracondylar region at right angles to the axial line of the femur so that correct apposition of the fragments may be had in both the anteroposterior and lateral positions, is the important factor in its application. To date we have experienced no evidence of infection, necrosis, or osteomyelitis.

Certain of our fractures of the lower third, with posterior displacement of the upper end of the lower fragment, developed evidence of circulatory obstruction of the lower extremity. Traction and manipulation in this instance was associated with great danger to the popliteal vessels. Open reduction in several cases showed sharp bony spicules engaging the outer vascular coats. These were carefully released without damage to the artery thereby preventing the development of gangrene and subsequent amputation.

During the past 2 years, the application of the Anderson direct skeletal traction splint for reduction of fracture of the neck has proved quite satisfactory. The insertion of the pin into the tibia, as described in the original article, has produced much discomfort about the knee, and following removal of the splint, there was noted some instability of the lateral ligaments. We have found that a more useful and comfortable method can be had by inserting a more stable pin through the condyles of the femur thereby avoiding traction upon the knee and permitting direct leverage of the lower fragment, which affords better opportunity for good apposition.

However, the ultimate realization of the cardinal principles of good union is, namely, firm approximation of the fragments with permanent fixation. This holds true perhaps more in fracture of the neck than elsewhere in the bony anatomy. Fracture of the neck of the femur still remains as pointed out by Speed, the unsolved fracture. In view of our unsettled knowledge of the vascular disturbance and the unsolved pathological changes in fracture of the neck, we should follow the precepts of standard methods and produce, if possible, firm apposition and permanent fixed retention. The preliminary application of the Anderson splint to establish length simplifies the procedure of open reduction at a later date. We prefer either the modified bone wire peg of Henderson or the Smith-Petersen flanged nail. The uncertainty of union in fracture of the neck, within a reasonable period of convalescence, has stimulated our interest in the value of a prolonged convalescent period which increases with age. We feel that a complete transformation period of absorption, re-establishment of circulation, and repair should develop before the weight bearing period is definitely established.

Our best results in intertrochanteric fracture have been obtained by the Anderson extension method. The excellent blood supply in this area favors good union when approximation is established.

Fracture of the shaft of the femur constitutes the greatest number of our series. We find a wide range of varieties occurring among all ages, but chiefly during the third and fourth decades, which we believe has cast a favorable influence upon our results.

During our early years, the methods of reduction were few. Amputation, deformities, and disabilities passed along without explanation or apology. The mortality of open reduction occasioned too great apprehension for its general recommendation.

The demand of the times, however, has developed a keen reconstructive interest among our

geons, notably the Fracture Committee of the American College of Surgeons, who have accomplished much to standardize the various forms of treatment

We have endeavored to establish, during the first 2 days, a method which will promote permanent fixation The early application of well applied adhesive extension with 30 or 40 pounds weight over a pulley, molding by coaptation splints, suspension in a Thomas appliance, are sufficient at times to obtain complete length, good alinement, and approximation in badly comminuted fractures Extensive comminution, we have found, favors early and rapid development of callus Not infrequently in this type, we find evidence of interposing fragments which delays or prevents the development of union The importance of early recognition in such conditions cannot be overemphasized, and early surgical intervention is clearly indicated in order to avoid delayed or non-union

The extension method with the aid of the Steinmann pin or Kirschner wire has not proved so satisfactory in fractures of the middle or upper third In supracondylar and displaced fractures of the lower third, our results have been quite gratifying

The many advances which have developed in the open method of reduction within recent years have established its position among the standard methods We do not consider this procedure a routine measure but reserve its selection in the treatment of acute fractures, when we fail to accomplish good coaptation and retention by the closed or other conservative methods The selection of open reduction in acute fractures should be established at a timely period before the regenerative properties of the bony and soft tissues have become exhausted Delay in open reduction is costly and reflects unfavorably upon the real value of the method

The uncertainty of the plaster cast as a sole permanent, retentive, and fixative agent in fractures of the shaft precludes its use as a reliable method of treatment

We have endeavored to perfect a simplified technique for open reduction which will assure an orderly operation with speed and safety The improvement in our technique has been in the institution of certain important measures the Hawley table, nitrous oxide oxygen anesthesia with carbon dioxide reventilation, standardization of instruments, and blood pressure observations during the operative procedure

The advantages of the Hawley extension table in open reduction of the femur are numerous Following careful adjustment of the patient to the table, the entire field of operation is prepared, before the administration of the anesthetic Following exposure of the fracture, reduction and correct approximation can be had by gentle mechanical traction, which reduces traumatism of tissues to a minimum.

The selection of the type of anesthesia is of great importance with reference to the various contributory factors in the development of shock. In 103 open reductions, the following types of anesthesia were administered ether, 23, nitrous oxide oxygen with carbon dioxide combination, 78, spinal, 2 The advent of complete nitrous oxide oxygen anesthesia on our service in 1921 for open reduction of fracture of the femur was an important acquisition in the prevention of shock

The third factor of importance includes the perfection of a properly systematized technique during the operative period, by which the operator can conduct the procedure without interruption The selection of a few simple, yet useful instruments, which the operator can handle with ease, has always been our desire This practice has simplified the difficulties of attempting correct approximation and has permitted the application of the fixative agent with a minimum disturbance to the bony and soft structures We have confined our fixative agents to bone grafts, wire, and the Sherman vanadium bone plate In badly comminuted fractures with displacement when open reduction is indicated, the use of wire and plate has been found useful In non-union the use of a properly secured bone graft has given us almost perfect results In a majority of cases we have favored the vanadium or alloy bone plate which can be easily fixed, if temporarily secured to the shaft by a Lowman bone clamp The insertion of the screws can then be performed rapidly by means of a special gauge screw which corresponds exactly to the size of the drill bit. Each screw has been previously attached to a retentive screw driver in order to expedite its application The soft parts about the site of fracture, including the fragments, are handled carefully and disturbed as little as possible except for the excision of interposing muscle or ligamentous tissue This is a frequent finding and undoubtedly a factor in the failure of reduction by the closed method In delayed reduction, one finds a rapid transition of the interposing muscular tissue into dense firm fibrous bands

Excessive traumatism and disturbance of the early reparative mechanism of the tissues, which is difficult to avoid in open reductions in delayed

TABLE I.—SUMMARY OF 278 CASES

Decade Age in years	Cases	Month	Cases	Year	Cases
[illegible]	[illegible]	January	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	February	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	March	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	April	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	May	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	June	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	July	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	August	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	September	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	October	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	November	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	December	[illegible]	[illegible]	[illegible]
Unknown	[illegible]				
Total	278	Total	278	Total	278

cases, have been attended by certain delays in the formation of callus development.

Rather than prolong the operative period by the application of plaster we have found sufficient protection by the use of the Thomas splint. The lower leg is fixed below by an already applied adhesive extension, and coaptation splints are applied to the thigh for additional protection

The fourth factor mentioned, namely blood pressure observations during the operation, has been found of great value as an index for the early detection of shock Observations are taken immediately before and throughout the operation every 2 to 4 minutes These observations show the usual high systolic rise during the preliminary stages of the anesthesia Certain activities at the site of fracture occasioned by extension of the limb manipulation of the fragments, curettement or chiselling of old callus drilling of the bone insertion of the screws, will influence the vasomotor mechanism according to the degree of activity This reaction will immediately record a fall, first, of the systolic and later the diastolic pressure These important observations denoting the presence of shock, even before the physical appearance of it is apparent, have been found constant in many cases The operative activities cease at this point until the patient has convalesced from shock Recovery may require several days before reduction can be completed with safety

These factors particularly the latter one, have not only afforded opportunities for better results but have favorably influenced our mortality rate in open reduction

In our series of 278 cases, 15 fractures were found to be compound The percentage is quite low as compared with fractures of the tibia, fibula, and upper extremities. As a rule there is no great destruction of soft tissue as frequently found in the tibia, unless the injury has been of a direct massive character A number were small puncture wounds which developed from within out and which always lessen the possibility of internal contamination. In the more extensive type with destruction of the soft parts and exposure of the fragments, we favor immediate open reduction, provided the condition of the patient permits For many years we have practiced immediate permanent fixation of the fragments, sensible débridement and open exposure of the wound by the application of a self-retaining retractor rubber tube drainage is inserted between the separated muscle bundles followed by the application of a loose gauze pack for the wound. An abundance of gauze is applied to the entire limb and it remains *status quo* for a period of 2 to 4 weeks

During this period the temperature subsides, the local reaction recedes, and there is a profuse foul smelling discharge but much to one's surprise a healthy granulating wound is observed upon the first dressing, even though a culture of the discharge may show several varieties of pathogenic organisms The care of the wound continues in this manner with infrequent dressings and its reparative nature progresses without active infection or any interference of callus formation This method is in many respects similar to the procedure advocated by Orr and has been a method of procedure in many of our compound fractures since 1916 In selective cases chloramin tion of the wound proved of value in certain others, larval therapy was efficacious

SUMMARY OF CASES

A brief summary of our cases including fractures of the entire shaft of the femur presents many interesting phases Since 1916 we have treated 278 consecutive cases of which 144 occurred in the third and fourth decades of life

We find a definite seasonal variation of occurrence of coal mine accidents, showing an increase during the warm months In our series the majority occurred during the month of July

It is of interest to note the various types of fracture as to location resulting chiefly by direct violence from falls of coal, slate, and posts Fractures of the shaft with the middle third predominating occurred most frequently 191 followed by fractures of the neck, 42 intertrochanteric 11 supracondylar 10 intra-articular involving the knee 7 double fractures, 7 exact site of shaft unknown, as result of early death without X-ray study 10.

TABLE II —TYPES OF FRACTURE AS TO LOCATION

Site of fracture	Cases
Fracture of neck	42
Intertrochanteric	11
Shaft—Upper third	51
Middle third	99
Lower third	41
Supracondylar	10
Intra articular of knee	7
Double fractures	7
Location unknown	10
Total	278

An attempt to standardize the average number of X-ray series including all views for a complete study throughout the entire period of treatment, is rather difficult, however, the records shown in Table III afford a fairly accurate average by excluding 20 X-rays in certain deaths which occurred shortly after admission

The selection of the fixative agent, we find, depends upon the character and location of the fracture For many years we have favored the Sherman vanadium bone plate Its application to the femur represents a high percentage of unabsorbable foreign substance and interferes in certain cases with the local formation of callus The simplicity of application and the firmness and security of apposition when correctly inserted have outbalanced certain criticisms which have been offered against its use In our series of 103 open reductions, 82 bone plates have been used In 9 cases, or 11 1 per cent, their removal was indicated for various reasons Other types of internal fixative agents were used when especially indicated In the series reported, the following fixatives were employed bone graft, 3, wire, 11, nail, 5, screws, 1, and no retentive appliance, 3

Cases of delayed and non-union were 3 and 5, respectively, in the entire series of 278 cases

The presence of local wound infection in our series of 103 operative cases fortunately was low Five wounds were involved, 2 of which developed septicemia resulting in death The 3 remaining were entirely local, 1 of which definitely delayed union

A summary of our mortality tables (Table V) has proved very interesting and undoubtedly will be of great assistance in our future work. In a total of 278 cases there were 32 deaths, or 11 5 per cent. Included in this series are many patients who died a few hours following admission to the hospital

Our records indicate that 21 died within 5 days after admission, 18 within 2 days, 13 within 24 hours, 9 within 8 hours, and 7 within 5 hours after admission A considerable number of these patients had sustained severe associated injuries, which not only delayed the employment of adequate local surgical measures but were direct contributors to the cause of death

TABLE III —SUMMARY OF AVERAGE X-RAY SERIES PER CAPITA

	Total X rays	Average per patient
Non-operative cases		
1916–1925	147	1 9
1925–1935	296	4 1
Operative cases		
1916–1926	136	3 5
1925–1935	258	4 4

TABLE IV —CAUSES OF POSTOPERATIVE DEATHS

	Cases
Shock, embolic	3
Septicemia	2
Total	5

The non-operative cases total 175 with a mortality of 27 or 15 4 per cent This rather high percentage was influenced, as noted, by the great number who died shortly following admission

The operative cases, which total 103, showed a death rate of 4 5 per cent Included in this group are 2 cases of fracture of the shaft, 2 confined to the neck, and 1 of both neck and shaft on opposite limbs The cause of death in 3 was attributed to postoperative shock of an embolic type, the remaining 2 developed septicemia some time following the operation from wound infection

The general causes of death, as found in Table VI, show that shock of various types and toxemias as the result of acute infections, are the major factors Other causes as noted, namely, coronary occlusion, circulatory failure, uremia, and pulmonary embolism occur infrequently

The primary desire of every surgeon undoubtedly is to save the life of his patient Second in importance is the rehabilitation of the injured individual, so that he may again assume his productive position in society at an early date The hospital service extended to our patients by the employer includes, in addition to the treatment of their acute illnesses, complete physiotherapy which not only hastens their return of function but is decidedly beneficial to their employer

A review of our series with reference to hospital confinement and total convalescence shows an average of 110 2 days and 252 3 days, respectively The average hospital confinement of closed reduction was 95 6 days, for total convalescence was 213 7 days The average hospital confine-

TABLE V—SUMMARY

No. and Time in hospital	Type of fracture	Associated injuries	Complications	Cause of death	Operative treatment
5 hrs.	Simple neck	Fracture pelvis, chest, humerus	Trauma, shock, ileus	Traumatic shock	No
3 da.	Simple comminuted middle /3	Fracture scapula	Lobar pneumonia	Lobar pneumonia	No
3 hrs.	Simple comminuted middle /3	Fracture skull, left rib, nose, fibre vertebra	Shock, hemorrhage	Shock, hemorrhage	No
3 mos.	Compound lower /3	Fracture dislocation hip, frac. vertebra	Shock	Traumatic shock	No
15 hrs.	Simple lower /3	Traumatic separation foot, compound fracture tibia—Lung point	Shock, hemorrhage	Shock, hemorrhage	No
6 da.	Old unreduced upper /		Shock, post-operative	Shock, hemorrhage	No
1 hr.	Compound comminuted lower /3		Shock, hemorrhage	Shock, embolus	No
19 da.	Simple comminuted middle /3	Fracture scapula, ribs, pelvis, vertebra, shoulder	Pneumonia	Shock, hemorrhage	Yes
4 da.	Simple neck	Contusion back, laceration scalp	Pneumonia	Infectional pneumonia	No
9 da.	Simple comminuted upper /3	Laceration scalp and cheek	Shock, ileus, pneumonia	Infectional pneumonia	No
21 da.	Simple comminuted middle /3		Infection wound, septicemia	Hypostatic pneumonia	No
4 hrs.	Simple neck	Compound pneumonia, dislocation hip, fracture ankle	Gas bacillus, shock	Septic pneumonia, septicemia	No
1 hr.	Compound lower /3		Shock, ileus	Trauma, acute shock	Yes
9 da.	Simple middle /	Fracture skull, laceration wrist	Shock, embolism—Cardiac and pulmonary	Traumatic shock	No
1 hr.	Simple middle /3	Fracture skull, nose, orbit, jaw	Traumatic shock, ileus	Shock, embolus	No
14 da.	Simple lower /3	Fracture pelvis, clavicle	Cerebral compression	Traumatic shock	Yes
7 hrs.	Simple middle /	Laceration scalp, shoulder	Shock, embolism—Cardiac and pulmonary	Shock, cerebral compression	No
14 da.	Simple neck	Fracture vertebra, tibia, ankle	Septicemia	Shock, embolism	No
10 da.	Simple upper /3	Laceration arm and orbit		Coronary occlusion	No
30 da.	Simple anterior/posterior	Fracture pelvis, chest, clavicle	Shock, ileus	Septicemia	No
11 da.	Simple middle /	Crush of chest	Carbuncle, Furuncle disease	Embolism—pulmonary	Yes
7 da.	Simple neck	Fracture pelvis, vertebra, femur	Hemorrhage	Traumatic shock	No
4 hrs.	Simple upper /3		Cerebrovascular failure	Coronary failure	No
12 da.	Simple lower /3 R L	Compound crush tibia	Shock, hemorrhage	Shock, hemorrhage	No
14 da.	Simple middle /3	Fracture femur, internal injury	Shock, embolism	Uremia	No
7 hrs.	Compound middle /3 L	Fracture ribs, crush of chest, rupture intestine	Hemorrhage	Shock, hemorrhage	No
14 da.	Compound upper /3 R		Pneumonia	Shock, embolism	No
8 hrs.	Simple neck	Crush chest, vertebra, abdomen, shoulder	Shock, embolism—pulmonary	Pneumonia, tetanus	No
8 hrs.	Compound middle /	Crush vertebra, abdomen, shoulder	Shock	Shock	Yes
30 da.	Compound lower /3		Shock, embolism—pulmonary and cerebral	Shock, embolism	Yes
11 da.	Compound lower /		Acute alcoholism, ileus	Shock, embolism—pulmonary and uremic	No
11 da.	Simple lower /3		Acute alcoholism, ileus	Shock, embolism—pulmonary and uremic	No
da.			Pneumonia	Cerebrovascular failure	No
				Infectional pneumonia	No

Before operation, 4 days.
Before cross bars, 14 days.

Summary	Cases	Per cent
Total fractures of femur	278	
Deaths	31	
Non-operative cases	77	
Deaths	7	
Operative cases	201	
Deaths	24	

TABLE VI —SUMMARY OF THE CAUSE OF 32 DEATHS

	Cases
Shock	
Traumatic	5
Hemorrhage	5
Embolic	7
Cerebral compression	1
Toxemia	
Lobar pneumonia	1
Influenzal pneumonia	3
Hypostatic pneumonia	1
Septicemia	2
Gas bacillus	1
Peritonitis	1
Other causes	
Coronary occlusion	1
Circulatory failure	2
Uremia	1
Pulmonary embolism	1

ment for open reduction was 134 8 days, total convalescence for open reduction was 266 6 days

The evident disparity noted in the cases without operation as compared with the ones with, is to be explained by the fact that the group treated by closed reduction includes not only those patients who died shortly following admission but also those with the less grossly displaced fractures of the femur

We have endeavored in this discussion to indicate the interesting factors in the progress of our work with the hope that it may contribute something of value in the standardization of treatment

In conclusion, it has been the authors' hope and intent to present an impartial review of 278 fractures of the femur The methods of therapy have at all times been held flexible Improvements in technique have been accepted and utilized in every instance when found applicable to the given case and within the scope of our talents At no time has stereotyped procedure been employed or advised, rather, it would seem to be the dictum of experience to allow each case to warrant the particular measure of care it may best accept

TABLE VII.—AVERAGE HOSPITALIZATION AND CONVALESCENT PERIODS IN DAYS, 278 CASES

	Average days
Average hospital days	110 2
Average hospital days of closed reduction	95 6
Average hospital days of open reduction	134 8
Average convalescence	252 3
Average convalescence of closed reduction	213 7
Average convalescence of open reduction	266 6

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FENDER FRACTURES[1]

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THE so called fender fracture is a comminuted compression fracture of the outer tuberosity of the tibia produced by a force exerted from the outer side which causes valgus strain.

In an accident of the sort here concerned the luckless pedestrian, standing with his leg straight in the moment of stress, is struck from the outer side by fender mudguard, or tire. The blow is received at or below the knee and forces the leg into valgus position that is a knock knee position. Something must give way The lower end of the femur as a whole may break, the internal condyle may be torn loose or the internal lateral ligament may be torn But in practice and in fact usually it is found that the external condyle of the femur is driven down and so crushes and displaces the outer side of the tibia outward and downward As a rule the break is such that the articular seat of the fibula, and with it the fibular head, moves outward and down with the fragments of the shattered tibia Uncommonly the fibula is broken also. The details vary Sometimes there is, or seems to be a single large fragment of tibia displaced en masse Oftener there is much and obvious comminution which extends to or through the joint cartilage

Often the comminution is much more extensive than the \ ray film indicates, and on account of the comminution and the consequent impossibility of satisfactory reduction and maintenance, I think it is fair to say that those who have seen many of these cases have come to regard open operation as not the method of choice but rather one to be avoided

The essential feature of this injury is the crushing down of the weight bearing surface of the tibia on the outer side This fact alone justifies its classification as a separate entity

The problem is to restore this weight bearing area to mechanical function as best we can In this task the handicaps are the muscle pull of the outer hamstrings, and later the stress of weight bearing In many cases, however not all of the tuberosity is crushed usually the back half is the part most seriously affected Even with the best \-ray films it is difficult to determine the precise amount of injury probably because part of the surface is intact It is for this reason, perhaps, that the clinical results in these fractures, when recognized and treated, are amazingly better than would be expected conversely the results in such fractures when not recognized or when treatment is bungled are amazingly bad, incredibly bad, for the patient may be left with extreme knock knee and a loose useless joint.

Clinical examination reveals an obvious genu valgum of varying degree with more or less outward lateral mobility and unless studied further the fracture is often overlooked. The \-ray film shows a picture which is not unusual It is noted that the fracture is a ragged one as a rule with a crushing down of the outer side of the tibia which has been driven down by the impact of the more solid outer femoral condyle. The tibial fragment, or oftener fragments, are driven outward and downward, thus giving place to the outer condyle of the femur Usually the upper end of the fibula is displaced outward also

It is evident that there are two sorts of injury In one one main fragment seems to be driven outward, a picture that tempts the surgeon to do an open operation It is true however, that replacement of such a fragment is done far better by impaction from without, since the spiking or screwing fast of the fragment is difficult because the bone is friable and therefore not strong enough to hold screws In the other type of fracture the comminuted type it is obvious that any fixation after the joint is opened is impossible.

The argument that one should do an open operation because there is a probability of later trouble with the semilunar cartilage seems a poor one to me I have heard of later displacements of the cartilage, but in a large series of cases I have seen no such trouble As to removal of the cartilage, it seems clear that if ever the cartilage is needed It is in these cases to maintain an articular surface and with its actual bulk to fill space. So that I am entirely against open operation, and although I have done it often, I shall probably never do it again Better reductions with more prompt healing and better final results can be obtained without open operation

The problem of caring for fender fractures is really a rather simple one First with patient under anesthesia, a space on the outer side of the joint is opened up by bringing the leg into over correction, which means it is placed in as near a bow-leg position as can be contrived with reasonable force Next the displaced fragments are pushed as nearly as possible into their normal positions This maneuver involves pushing the

[1] Presented at the Symposium on Fractures, before the General Congress of the American College of Surgeons, San Francisco October 30–November 4, 1927

fibula inward as well Much can be done with strong thumbs Some surgeons use screw pressure with a furniture clamp or its equivalent. Personally if thumbs seem inadequate, I am apt to use a hammer The knee is protected with a felt pad, and the blow or blows are delivered close to the joint over the broken condyle and the upper front of the fibular head In this way any possible damage to the external popliteal nerve, in its curve about the fibular neck, is avoided The method works and has the advantage that the force of the blow may be delivered upward as well as inward, which is what is wanted There has been no case of local damage as the result of the pounding, and the reduction of the fragments seems to be as accurate if not more accurate than that produced by any other method Perfect restitution is, of course, never attained, but adequate repair and function do not seem to require it

The next problem is the maintenance of reduction It must be remembered that an instant's relaxation in the correction of the leg as a whole means disaster and the reproduction of the original deformity by muscle pull Therefore, a close fitting plaster cast is essential The cast is molded to give pressure outward on the inner side of the knee and inward on the lower part of the lower leg In addition moderate pressure over the broken condyle probably helps After 3 weeks, gentle motion is begun but with the leg supported or hanging straight After a month, a caliper splint which gives support by padded plates at the indicated points may be worn by day and the plaster cast at night After the lapse of 5 or 6 weeks, weight bearing with the splint is permitted Unsupported weight bearing should not be allowed earlier than 12 or 14 weeks after the injury The end-results depend mainly on the thoroughness of treatment With the treatment just outlined, there should be no unstable joints

Motion of the joint to a right angle or better may be counted on, the mobility varying from that point to an absolutely normal motion Broadly speaking, however, some loss of knee flexion results, but stable, strong, painless joints are secured If fractures of this type are not reduced or are poorly reduced there result a conspicuous genu valgum and some, often great, lateral instability, which necessitate such relief as can be obtained by supracondylar osteotomy and correction of the weight bearing line

In conclusion I would make a plea for the careful study of fender fractures so common in these days of auto traffic injuries so that they may be recognized and treated as a real fracture entity This injury, so often underestimated as to its seriousness, needs and greatly merits real study and most thoroughgoing care

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LOCAL ANESTHESIA IN FRACTURES[1]

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DURING the past 15 years, ending December 31, 1934, we have treated at our private clinic 5,910 fractures. The diagnosis of every fracture was confirmed by an X-ray film and a complete record and follow up has been made of every fracture.

As a pupil and for many years an enthusiastic admirer of the monumental Rudolph Matas, of New Orleans, I necessarily have been keenly interested all my professional life in local, infiltration, and regional anesthesia. Even as a student in dear old Charity Hospital in New Orleans, I was amazed and thrilled to see Professor Matas resect the superior and inferior maxilla under local and regional anesthesia, amputate arms and legs, and resect joints. Thus, I have always set fractures and reduced dislocations of phalanges and metacarpal and metatarsal bones under infiltration and regional anesthesia. Also, in open operations for reduction of fracture of the radius and ulna, tibia and fibula, and fractured patella in 75 per cent of the cases operations have been done under local and regional anesthesia. In operations on the skull for depressed fractures, for compound fracture of the skull, for extradural and subdural hemorrhage, we have preferably used for many years, infiltration anesthesia.

However it was not until the fall of 1927 while watching the practical, ingenious Lorenz Boehler in his clinic in Vienna, inject a 2 per cent novocain solution between the ends of the broken bone and secure, in a few minutes perfect analgesia and perfect muscle relaxation, that lasted usually from 1 to 1½ hours, that I realized what a marvelous adjunct to the treatment of fractures we had in local anesthesia. I was not impressed, however with nor have I been enthusiastic about, the use of regional anesthesia for setting fractures of long bones and for reducing dislocations of large joints as practiced in Boehler's clinic. I believe that ether anesthesia is more practical and safer in the majority of such cases.

Every doctor who treats or may treat fractured bones should familiarize himself with the simple and safe method of producing complete analgesia at the site of fracture and complete muscular relaxation, by injecting from 5 to 50 cubic centimeters of 2 per cent sterile novocain in normal saline solution directly into the hematoma or blood pool between the ends of the broken bone or bones. If the hematoma is present and the 2 per cent novocain solution has been injected into the blood pool, complete analgesia will occur in about 10 minutes and will last from 1 to 1½ hours. If there is no definite hematoma because the fracture is of the impacted or greenstick variety then it will be necessary to inject the solution into the muscular tissue adjoining the fractured ends and also under the periosteum to get analgesia and relaxation. In other words, to use infiltration anesthesia.

Anesthesia used. In our clinic we have used 2 per cent solution of novocain in normal saline. The amount varies from 5 to 50 cubic centimeters, but after injecting 25 cubic centimeters we watch the patient carefully for toxic symptoms. We have never had a death from novocain poisoning, but we do occasionally get toxic symptoms in infiltration anesthesia when using more than 10 cubic centimeters of 2 per cent novocain solution, so this strength solution must not be considered entirely harmless.

Technique of injection and paraphernalia necessary. The instruments and materials needed are, one 10 cubic centimeter glass syringe, 1 fine needle and 1 long medium shaft needle, 1 hemostatic forceps, 2 per cent novocain solution in normal saline, ether and iodine, cotton applicator and gauze.

The operation must be carried out with most meticulous regard for surgical asepsis—and this precaution is so easily quickly and economically taken care of with the simple equipment just named. An outfit of this description should be carried as a sterile fracture package in the surgical kit of every doctor who does or may do, fracture work. In our clinic all fractures are treated as an immediate emergency whether the patient is admitted during the day or at night. An X-ray picture is made at once. If in our judgment the fracture should be reduced under local anesthesia, if it is a simple fracture, the site of the fracture or fractures is noted on the X-ray film and then verified by palpation with the finger. The area is cleansed with ether and a small area is painted with iodine; at this site a wheal is made with the fine needle, a forceps, of course being used to apply the needle to the syringe, and the soft tissues to the bone are injected slowly and gently so as to avoid pain. The long needle is then attached and an attempt is made to locate the hematoma surrounding the ends of the broken

[1]Presented in the Symposium on Fracture before the Clinical Congress of the American College of Surgeons, San Francisco, October 28–November [illegible], 1935.

bone or bones When the hematoma is found, by slight suction or without suction, a light colored fluid is aspirated into the syringe, then the 2 per cent novocain solution is slowly injected into the blood pool If the blood is from a vein it will be much darker than the fluid from the hematoma Injection is continued without withdrawal of the needle until there is analgesia and complete muscular relaxation, or marked tension of the tissues from the infiltrating solution When the needle is withdrawn, the opening is sealed with gauze and kept sealed until the fracture has been reduced

Many years ago, a dentist gave me an inspiration about local anesthesia He had the reputation of doing dental work without pain I called to see him and noted that after making his anesthetic injection, he left this patient to work on another patient, thus giving the anesthetic time to deaden the tissues Reduction should not be attempted under 10 minutes, and often the analgesia and relaxation is not complete until 30 minutes have elapsed Relaxation and analgesia thus secured will last from 1 hour to 1½ hours The more one uses this method, the more enthusiastic he will become, as there is so little pain and discomfort, such perfect relaxation of muscles, and usually such ease of reduction

Indication Local anesthesia can be used in all fractures, even compound, except fractures of the spine and the pelvis Age is no contra-indication

Advantages An assistant is not necessary and, in isolated areas, the patient is saved much suffering and long waiting until an assistant can be called to give a general anesthetic It allows for repeated manipulation without the necessity for a second anesthesia or a long continued anesthesia If the fracture is associated with brain trauma, as so many of the fractures due to automobile accidents are, and a general anesthetic cannot be given, local anesthesia must be used Too, when there is profound shock, general anesthesia cannot be used, but local anesthesia can often be used and will actually lessen shock by relieving the pain of the jagged end of bones mutilating the soft parts Most patients are profoundly grateful for the local anesthesia and will co-operate fully and helpfully as so many have a horror of being put to sleep

In our clinic every fracture is treated as an individual case and not by any set rule, formula, or standard We study the fracture on the X-ray film, we study the patient, the surroundings, and then we decide whether we shall use local anesthesia, nitrous oxide gas and oxygen, or ether anesthesia We are profoundly impressed with the marvelously safe and simple method of reducing fractures by injecting a 2 per cent novocain solution into the hematoma surrounding the broken ends of bones, but we are still using nitrous oxide gas and oxygen and ether anesthesia for reduction of fractures We will continue to use that method of anesthesia which seems best adapted to the particular patient, time, and conditions present

AIRWAY AND HIGHWAY FIRST AID STATIONS[1]

E. PAYNE PALMER, M.D., F.A.C.S., PHOENIX, ARIZONA

SINCE July, 1931, I have laid my plans before many agencies for the establishment of first aid stations in the United States. In 1933 I interested the American Red Cross in the setting up of first aid stations on the highways. At that time they endeavored to sponsor the movement. Unfortunately the general financial stringency prevented their backing the movement to any great extent.

Today the American Red Cross is willing and anxious to establish first aid stations on both the highways and the airways of our country. The officials at National Headquarters have just recently approved plans looking to the immediate establishment of first aid stations along our main traveled roads and at emergency landing fields and air ports. There are already 17 first aid and life saving field representatives of the Red Cross devoting their entire time to this work and 235 first aid stations are now operating in the United States. Definite arrangements have been made to open 432 additional stations within the next few weeks. Conservative estimate indicates that 1000 stations will be arranged for before July 1, 1936.

We in the United States are not alone in recognizing this need. For over a year Canada has maintained first aid posts between Toronto and Montreal. In the summer of 1934 more than 300 automobile injury cases were given first aid care by post attendants. The Belgian, French, and German Red Cross societies are actively supporting this same service on their highways. France, for example, has 2000 first aid stations operating successfully along the highways. The movement has been met everywhere with public approval and praise and the League of Red Cross Societies has appointed a permanent committee to consider this subject throughout the world.

At the present time we are not prepared to take care of injured travelers, and with an increasing toll of accidents we find before us a humanitarian duty that is at once neglected and urgent. Since the state and federal agencies have failed to provide means of giving first aid treatment to these injured travelers, it is apparently up to us—up to such a group as the Fellows of the American College of Surgeons—to stimulate the establishing of first aid stations where they are needed, to co-operate with the American Red Cross in seeing that these stations are equipped, and are properly maintained and operated. Since fractures occur in most accidents the Regional Fracture Committee should be especially interested. Even with the American Red Cross and the American College of Surgeons united in this work, it still cannot succeed unless we have community interest. Co-operation must be obtained from local medical societies, state highway patrols, automobile clubs, chambers of commerce, Boy Scouts of America, telephone companies, service and luncheon clubs, women's clubs, and in particular county officials.

Today we are spending millions in improving our highways and more millions in buying machines with greater speed and power. It is a deadly combination. During the year 1934 there were 35,769 automobile deaths, a 15 per cent gain over 1933. A million and a quarter people were injured in automobile accidents alone. Many of these accidents occur in remote and lonely places where there are no physicians, where there are no facilities for taking care of the injured. Consequently before trained assistance can be secured, prolonged suffering is bound to occur, to say nothing of the complications and sequelæ which retard recovery and of the deformities which not infrequently occur. In addition there is the ever present possibility of delay proving fatal to the injured person.

Preparedness, of course, is our first aim. Only then, when an airway or highway disaster occurs, can adequate emergency first aid be given to the injured person without delay. And it is possible to give a very effectual first aid service through the establishment of these first aid stations and through the training of the people in charge in first aid and fixed traction method of transportation of the injured.

The airway first aid stations should be established at the emergency landing fields as well as at established ports, as it is here that accidents are most apt to occur. At the regular landing fields, these stations will take care of such accidents as occur locally as well as of any injured passengers brought to the fields. Highway first aid stations will be established at remote places where medical care is not available, at important crossroads or other points where accidents are apt to occur frequently, and at convenient intervals along important roads in order to establish a continuous service on all through highways.

[1] Presented at the Symposium on Fractures, before the Clinical Congress of the American College of Surgeons, San Francisco, October 28-November 1, 1935.

Fortunately, filling stations are usually found at or near these sites and are operated by a good class of people, consequently they can usually be selected as highway first aid stations of the American Red Cross Wayside stores, residences, and farmhouses also can be designated as stations when it is deemed advisable The state highway patrol is in possession of valuable data that will be of use in the selection of sites on the highways A system of mobile first aid stations should likewise be placed in the public utility companies' trucks, and in other vehicles that ply regularly up and down the highways Trucks thus equipped will greatly expedite this service

The second consideration in the selection of the station is the ability and willingness of the proprietor and his helpers to give an effectual first aid service The permanency of the personnel of the stations is a third point to be taken in mind before deciding upon the site

By way of equipment, each station must keep on hand a sufficient quantity of first aid supplies such as is contained in the Red Cross kits a blanket, wooden splints, a Thomas-Murray upper extremity splint, a Keller-Blake lower extremity splint, and a stretcher There should also be two or more persons trained in administering first aid to the injured and fixed traction method of transportation available at all times at each station Day and night service should be operative If certain stations remain open only during the day, then they should display a sign giving the location of the nearest full time station

Care must be exercised in the selection and training of the first aiders They must not only be taught the administering of first aid but also their relationship to the injured person and to the physician who is to have charge of the case They must understand that first aid service is strictly an emergency measure, carried out after an accident in the absence of a physician, and that it is preparatory to medical care which must be given as soon as possible Only emergency first aid service required at the time of the accident is of course permissible, and all injured persons given first aid care must be seen by a physician

The First Aid Committee of the American Red Cross and the Regional Committee of the College should co-operate, and train those selected to serve at these stations An adequate training would be that provided in the American Red Cross regulations for first aid course of 15 hours of instruction, or its equivalent. In addition and of equal importance, there should be given a thorough instruction in fixed traction method of transportation for fractures, which is applied before the injured person is moved We should consider fractures as emergencies and the initial treatment as the most important Residents in the vicinity of the station then should be trained so that they can assist or act as principals in case of an emergency No charges are to be made for first aid service or supplies, and no gratuities allowed

A special accident report form has been prepared by the Red Cross, and a supply of these will be kept at each station to be filled out by the operator, giving an account of each person injured The stations should also be provided with a telephone, if possible, and either a medical directory or a list of the names of the nearest physicians and approved hospitals A sign lettered on both sides will occupy a prominent place designating each Red Cross first aid station Road markers indicating the location of the station will be placed a half mile away on each road leading to the station An organized volunteer automobile transportation service, if needed, should be established at or near each station, so that the injured may be transported to a physician's office or hospital Ambulances, passenger cars, and small trucks may be made available for this Again there will be no charge for the volunteer transportation of the injured, ambulance service, however, when necessary will be paid for by the injured

The approximate cost of equipping a station is about $30 00 The cost of the articles needed should be apportioned about as follows twenty-four unit Red Cross first aid kit, $6 25, Thomas-Murray splint, $1 25, Keller-Blake splint, $2 25, blanket, $5 00, stretcher, $6 00, station sign, $4 50, and two to four road markers, $2 25 each Four road markers of course will be needed if the station is located at an important crossroad Wooden splints can be made locally under the direction of the first aid committee member, and the annual upkeep should not exceed $10 00 There is no personnel cost in connection with this work as the entire service is on a volunteer basis, from the time that first aid is given until the injured person is delivered to a physician or a hospital Then and there the free service ends, and it will be expected that direct payment will be made to the physician and hospital for their services The cost of operating this service then will be slight and can be easily financed from the proceeds of the annual Red Cross roll call with such financial assistance as can be secured from other sources A plan now being worked out, if successful, would furnish the money for extending a network of stations over the entire country

The Chapter Executive Committee should take general responsibility and action upon the establishment of the first aid station. The direction of these stations should be given to the First Aid Committee. One member of the committee should be placed in charge of each station and made responsible for its operation. He in turn would co-operate with a member of the Regional Committee or a subcommittee member. Between them they would inspect each station at least once a month to see if the first aiders are maintaining an efficient service and keeping the first aid equipment in proper condition. At the same time they could arrange for the replacement of used materials and collect the accident reports for the Chapter Executive Committee. They would likewise check up on the volunteer transportation service, give instructions as to the disposition of the injured, and follow up accident cases to see that they have received proper care.

The state highway patrol also should be trained in first aid and fixed traction method of transportation by members of the First Aid Committee and Regional Committee. They should carry cards showing their capability to render first aid to the injured, a Red Cross kit, wooden splints, a Thomas-Murray splint, and a Keller Blake splint. They should frequently contact the first aid stations on their patrol. A display of interest in each station, its service, and the personnel's ability to use their equipment intelligently will do much toward helping maintain vigilant preparedness.

Accidents resulting in bruises, cuts and sprains can be given first aid easily. In case of fractures extreme care must be exercised in the first handling to avoid further injury to the bone and soft structure. Between one and one and a half million fractures occur in the United States each year, and many of them occur on the airways and highways. The medical profession must realize the need of and carry into effect more generally, the fixed traction method of transportation of fractures. Every doctor should be well trained in first aid and fixed traction so he can instruct the public in these methods and actively assist in carrying on this movement. The fixed traction method of transportation of the injured can be carried out very satisfactorily by a lay person after a short training and with the proper splint, thereby insuring protection to the fractured part and a reduction in the time of recovery. The Boy Scouts of America, the personnel of our regular army and first aid crews in factories and mines are usually so trained.

Since most of the airway and highway first aid in remote places is given by the laymen, they must be properly prepared to handle these cases when called upon to do so. The manner in which the injured person is splinted and transported is of first importance. Many a simple fracture has been converted into a compound fracture with severe damage done to the soft structure through improper first aid attention. On the other hand, it is estimated that there is an average saving of one hundred dollars in the treatment of each extremity fracture in which the fixed traction method is used. Were this method universal it would result in a saving of approximately thirty million dollars a year to the country as a whole.

When the stations are established, the chapter should announce through the newspapers that this activity is operative in that community. The article should then tell of the nature and the purpose of the service and the location of the stations. I am sure with the whole hearted co-operation of the American Red Cross, the American College of Surgeons, and the laity a network of first aid stations can be spread across the entire United States within a very few years at the most, stations equipped and qualified to give an efficient service to the injured travelers on the airways and on the highways. And when this is accomplished, it is not beyond the bounds of possibility that the mere presence of these stations will check our mounting toll of accidents. Certainly such stations will be an ever present warning to careless drivers.

CONFERENCE ON TRAUMATIC SURGERY

THE IMMEDIATE AND DELAYED TENDON REPAIR[1]

MICHAEL L MASON, M D, F A C S, CHICAGO, ILLINOIS

THE intelligent surgical repair of injured tendons is dependent upon a knowledge of the anatomical and physiological characteristics of this tissue This knowledge has developed as the result of the patient labors of many men[2] to whom we must acknowledge our great indebtedness The time at our disposal does not permit an extended discussion of the general development and extensive literature on the subject of tendon surgery We have gone into this on two previous occasions The papers of Sterling Bunnell, of San Francisco, have done so much to fashion our ideas of tendon repair both in this country and abroad, that they must be read by anyone who attempts to do this type of surgery

Tendon consists of long parallel strands of strong collagenous tissue, insecurely bound together by a sheath which sends into it fine septa dividing it into a number of separate bundles This binding tissue offers little resistance to separation and fraying of the fibers and makes poor anchorage for suture material The handling of tendons and the introduction of sutures into them require a careful and special technique, fine instruments, fine needles and thin strong sutures, and a method of suturing which secures a strong hold without disrupting the tendon, damaging its blood supply, or interfering with end-to-end union

Although poorly vascularized, the tendon receives its blood supply from three sources from the muscle proximally, from the periosteal insertion distally, and from tissues surrounding it along its course Tendons without synovial sheaths are surrounded by a specialized type of loose vascular areolar tissue, the paratenon, from which numerous blood vessels enter around the whole periphery Such tendons are relatively well supplied with blood, are relatively resistant to infection, and tend to heal relatively rapidly, although often in a lengthened condition if a reasonable approximation is obtained, and may even heal spontaneously if merely immobilized The sheath-enclosed tendons lie suspended in a synovial lined tube by a thin mesotenon through which a rather meager blood supply reaches them If the mesotenon is injured or destroyed, serious nutritional disturbances ensue, the tendon succumbs easily to infection and reparative processes are seriously retarded or even suppressed These tendons heal slowly, even under ideal conditions, and their surgical repair should be undertaken only when asepsis is assured and adequate facilities are available

A physiological factor which works both for and against the surgeon is muscular tonus with which is associated the phenomenon of tendon retraction Even with the relaxation obtained by splinting, the tendon is subjected to a constantly varying pull which exerts a force upon any suture line and, despite our best efforts, practically always leads to some separation of the stumps However, the suture line and the tissues bridging it across are subjected to a constant directional force which determines the lines of structural growth of the new tissue Without this force, our efforts at tendon repair would probably be fruitless

The amount of retraction of the proximal stump varies with the length of the muscle tendon and the nature of the surrounding tissues The longer the tendon and the more tortuous its course, the farther it retracts Tendons within synovial sheaths retract much farther than paratenon covered tendons Immediately after division, the proximal stump can be brought down If, however, the retraction is allowed to persist, permanent shortening occurs and, for this reason, primary suture is the procedure of choice However, since we are dealing with accidental injuries, we must weigh carefully the advantages of primary suture against the dangers of introducing infection into uncontaminated tissues in our search for the proximal stumps Under ideal conditions primary suture is justified, if such conditions do

[2] For a survey of the literature on the subject of tendon surgery with extensive bibliographic references, the following articles should be consulted HESSE, F Die Behandlung der Sehnenverletzungen. Ergebn. d Chir u Orthop., 1933 26 174–264. KOCH, S L. and MASON M L Division of nerves and tendons of the hand with a discussion of the surgical treatment and its results Surg., Gynec. & Obst., 1933, 56 1–39 MASON M L., and SHEARON, C. G The process of tendon repair an experimental study of tendon suture and tendon graft. Arch Surg., 1932, 25 615–692

[1] Presented in the Symposium on Industrial Medicine and Traumatic Surgery, before the Clinical Congress of the American College of Surgeons, San Francisco, October 28–November 1 1935

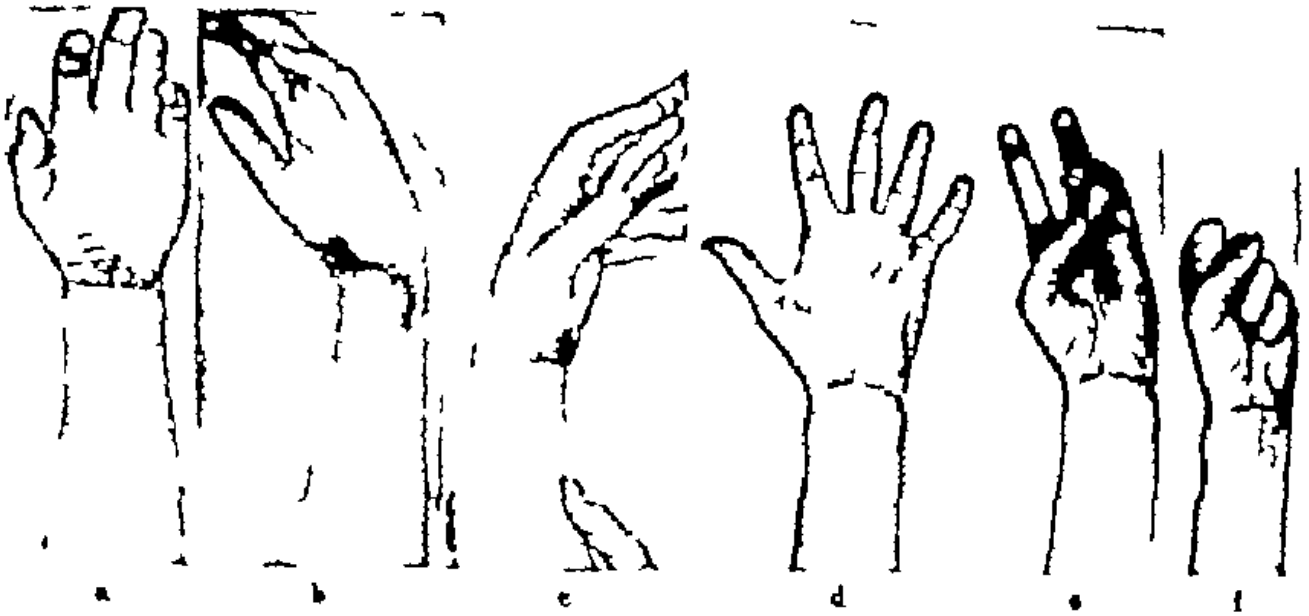

Fig. 1. Case. Primary nerve and tendon suture. Laceration occurred indoors. Division of median nerve, palmaris longus tendon, and sublimis tendon of the middle finger with partial division of the sublimis tendons of the ring and little fingers and of the flexor pollicis longus and flexor carpi ulnaris. Operation was performed 3 hours after injury. a, b, and c, Hand on the third postoperative day shows primary healing, with the wrist kept flexed to relieve tension on sutured structures. d, e, and f, Three months after operation, return of function is nearly complete. Of particular interest is the beginning restoration of rotation of the thumb.

not exist, it is better judgment to cleanse and close the wound, and then wait until healing has occurred before secondary suture is done under aseptic conditions. We have much to gain and only a few weeks' time to lose with such a course.

A study of the histology of tendon repair has shown two phases in the process. The first union between tendon ends is effected by the proliferation of connective tissues about and within the tendon. This proliferation begins a short time after suture and within a few days the stumps are fused in a fibroblastic splint. The second phase in the process is the repair which proceeds from the tendon itself, an actual proliferation of tendon cells across the gap. This proliferation can be seen as early as the fourth day after suture but it proceeds quite slowly and does not bridge the defect for from 10 to 14 days. As this tendon cell proliferation becomes an important factor in maintaining union, the sheath tissues begin again to assume their function as gliding tissues; they become areolar and lax, so as to permit gliding of the tendon.

The blood supply for tendon repair must, of necessity, come mainly from the contiguous tissues since the number of vessels traversing the tendon in a longitudinal direction is small, and the vascular flow is diminished by suture material. During the reparative process, it is well for the tendon to lie in contact with vascular and lax peritendinous tissues. If these tissues be dense and fibrous, bony and periosteal, the line of union or the tendon graft is certain to become firmly adherent and non-function results.

The immediate treatment rendered the patient with a tendon injury will depend upon two factors of practically equal importance. These are *the facilities available for carrying out proper* surgical repair and the condition of the wound.

The repair of divided tendons, whether in an apparently simple wound or in a very complicated injury, should never be attempted unless every facility for the most careful and non-hurried work is available. Tendon is so susceptible to infection that we feel that as great, possibly even greater care must be taken to obtain and preserve asepsis as in abdominal or intracranial surgery. The surgeon should not attempt these procedures without adequate trained assistance. Except in very rare cases, a general anesthetic will be required first, because of the length of time necessary to identify and repair the tendons and, second, because the blood pressure cuff applied to control bleeding becomes quite unbearable to the unanesthetized patient. The proper instruments—fine needles, sutures, retractors, and forceps—must be at hand; it is worse than useless to attempt the suture of fine tendons with the ordinary operating room equipment. Lastly the surgeon himself should be familiar with this type of surgery, should be conversant with the anatomical relations, and should have the patience to

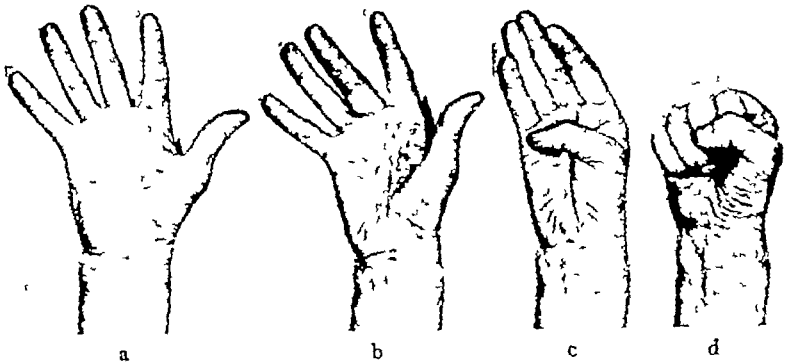

Fig 2 Case 2 Condition of hand 1 year after primary suture of completely divided median nerve, abductor pollicis longus, flexor carpi radialis and palmaris longus, and of partially divided flexor pollicis longus and flexor digitorum sublimis of the middle finger To be noted especially is the rotation and abduction of the thumb

go slowly and carefully about his work. Tendon surgery can neither be undertaken as a minor procedure sandwiched in between other operations, nor can it be relegated to untrained internes or house officers

The second factor to be considered is the condition of the wound itself Friedrich's experiments have shown that the time elapsing between the reception of an injury and the surgical care is of considerable moment. Within the first 6 hours after an injury the wound is contaminated, but is not as yet infected, since bacteria as found in dust, dirt, and other foreign matter, are not acclimated to the cultural requirements of human tissue During the time they are becoming adjusted, it is possible to remove them mechanically by washing and excision, thus rendering the wound relatively aseptic After this period of adjustment, of 6 to 8 hours, has passed, we must consider the tissues to be infected The sooner, therefore, a wound is seen and given care, the greater are our chances of obtaining primary healing Up to 6 or even 8 hours, most wounds can be cleansed, débrided, and closed In the case of tendons, suture should seldom be attempted in wounds over 4 hours old, we may cleanse, débride the wound, and close the skin, but we must leave tendon repair for a later date

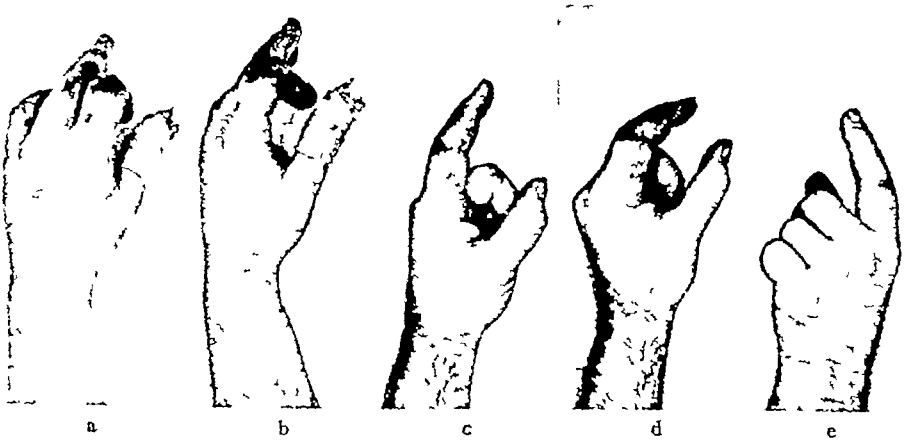

Fig 3 Case 3 Multiple lacerations and abrasions of the left hand due to an electric fan injury Immediate repair 1½ hours after injury a and b, Before operation. The most important injury is a division of the extensor tendon and joint capsule over the proximal interphalangeal joint of the index finger c, d, and e, Condition of the hand 6 weeks later Functional return well started in the index finger Patient was already back at work at time photograph was taken.

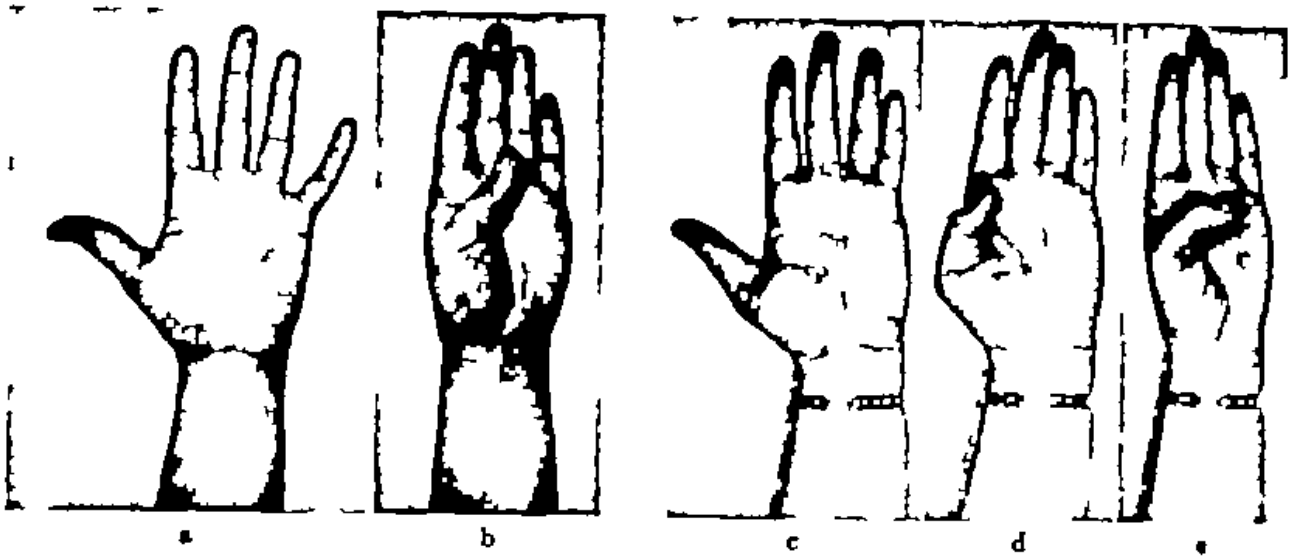

Fig 4 Case 4 Division of flexor pollicis longus at base of proximal phalanx, delayed suture 11 weeks after injury a, and b, Before operation the patient was unable to flex the distal phalanx of the thumb c, d, and e, Eight months after end-to-end suture There is practically complete restoration of function

The degree of contamination of the wound must be considered before tendon repair is undertaken. It is obviously impossible to establish definite criteria for wound contamination this is a matter of surgical judgment. Generally speaking, we can say that wounds received out-of-doors and grossly contaminated with street or garden dirt, are too dangerously soiled to allow tendon repair whereas wounds received indoors, or by clean objects, generally lend themselves to primary suture. The condition of the patient s hands at the time of the injury, and the nature of the first aid treatment should be ascertained. If the hands were grossly soiled, if rags or dirty handkerchiefs were used as dressings, if the wound was handled or explored without benefit of asepsis, it is usually better judgment to cleanse it thoroughly close the skin, and delay tendon repair

The nature of the divided tendon is of importance in the decision The paratenon-covered tendons, because of the lesser amount of retraction, greater resistance to infection, and greater tendency to heal, do very well with primary suture. The sheath-enclosed tendons on the dorsal and volar surfaces of the wrist, with long and fairly good mesotenons, heal pretty well after primary suture. In case of division of the flexor tendons on the volar surfaces of the fingers and thumb, experience is slowly teaching us that secondary repair is the wiser procedure.

The following brief case reports have been selected from recent cases of Dr Sumner L. Koch and myself at Passavant Memorial Hospital, to illustrate the criteria of decision between performing primary and secondary repair

Case 1. P H H Passavant Memorial Hospital, 7767 (April 29 to May 1 934). The patient, male, 31 years of age, slipped on a rug in his house and thrust his left hand through a glass door receiving a deep laceration of the left wrist. A tourniquet was applied at once a sterile dressing was placed over the laceration, and the patient rest at once to a doctor's office Here some novocain was injected, the wound was washed, iodine was applied to the skin, and the wound was explored with sterile instruments. The patient was then sent to Passavant Memorial Hospital for treatment. H arrived in the operating room 3 hours after the injury and under a general anesthetic, the hand and then the wound were thoroughly cleansed with liberal amounts of soap and water, and the injured structures identified There was found a complete division of the median nerve, the palmaris longus tendon, and the sublimus flexor tendon of the middle finger The sublimus flexors of the ring and little fingers, the flexor pollicis longus, and the flexor carpi ulnaris were partially divided. The incision was extended upward for a slight distance along the ulnar side of the forearm and the divided structures were sutured The tendons were first sutured, then the median nerve, and the wound was closed with fine silk sutures in the subcutaneous tissues, and dermal sutures in the skin. A splint was used to keep the wrist in moderate flexion and pressure dressing was applied. The wound healed by primary intention (Fig 1, a, b, c) and the patient was discharged on the third day Examination of the hand 3 months later showed beginning return of sensation over the area of median nerve distribution and that rotation of the thumb was returning (Fig 1 d, e, f) as further evidence of median nerve regeneration.

Case 2 M L., Passavant Memorial Hospital, 10244 (May to May 7 932) The patient, male, aged 30 years, received deep lacerations of the wrist on a jagged edge of 5 gallon water bottle which broke while he was pushing it across the floor He was brought within 5 minutes to the emergency room of Passavant Memorial Hospital, where the hand and wound were carefully washed and large sterile dressing was applied Examination revealed loss of sensation over the area of distribution of the median nerve and inability to rotate the thumb into opposition to the fingers. He was taken to the operating room, a general

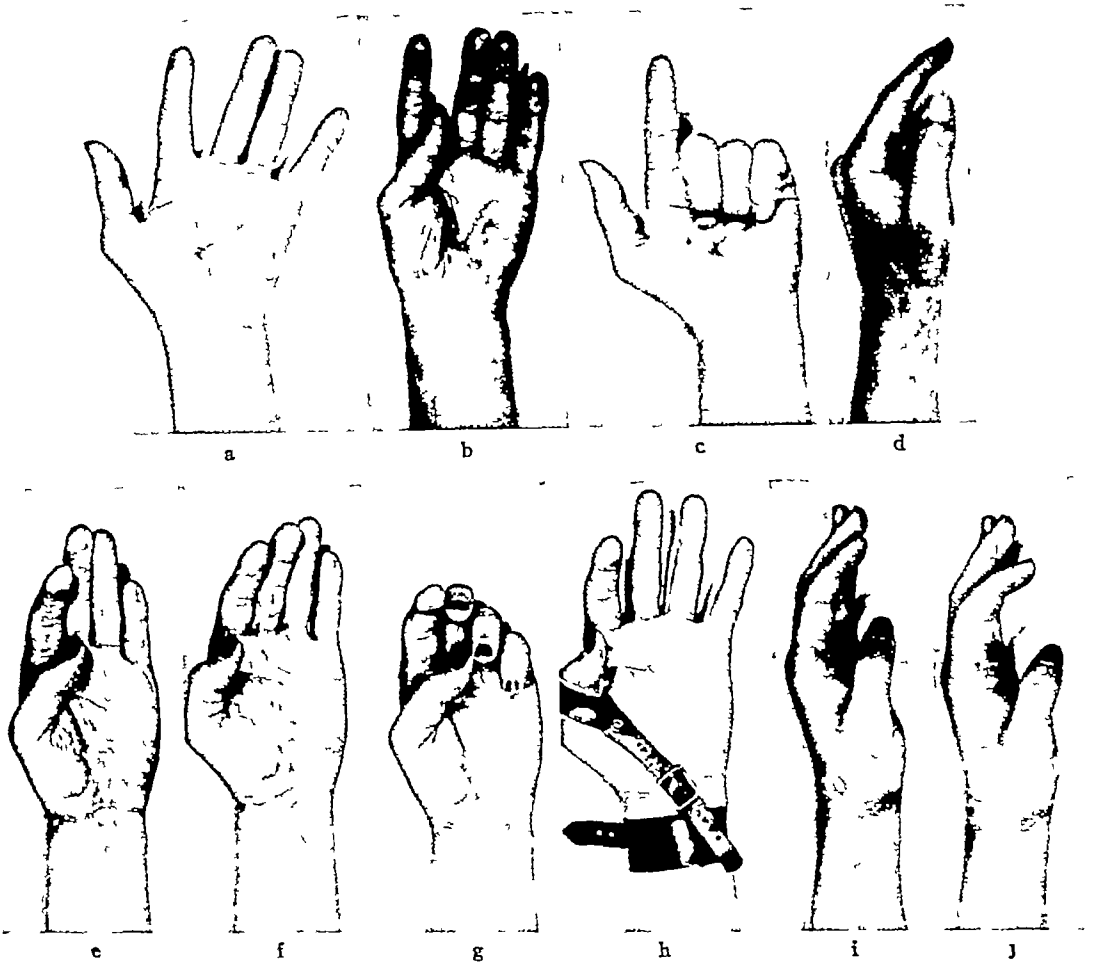

Fig 5 Case 5 Division of median nerve (partial), flexor pollicis longus, flexor digitorum profundus and sublimis of index finger on broken porcelain faucet 3 months previous to repair. a, b, c, and d, Condition of hand before operation. There is loss of flexion of the interphalangeal joints of the index finger and thumb, loss of rotation of the thumb, and sensory loss on the radial half of the palm and volar surfaces of the thumb and index finger and radial half of middle finger e, f, g, h, i, and j, One month after operation. Flexion is beginning to return in the thumb and index finger A strap has been fashioned to produce rotation of the thumb and relax the thenar muscles

anesthetic was administered, and the soap and water cleansing was repeated. There was found an almost transverse laceration of the radial two-thirds of the volar surface of the wrist with complete division of the abductor pollicis longus, flexor carpi radialis, palmaris longus, and median nerve. The flexor pollicis longus and flexor sublimis of the middle finger were found to have been partially divided. The divided tendons and nerve were sutured with fine silk, and the wound was closed with fine dermal sutures, the wrist was held in semiflexion on an aluminum splint and a pressure dressing was applied. Healing occurred by primary intention, and the patient was discharged on the sixth day after operation Examination of the hand 1 year later (Fig 2) showed good motor function, including returning power of rotation of the thumb

CASE 3 S C, Passavant Memorial Hospital, 18298 (June 11 to June 13, 1934) This patient, male, aged 28 years, injured his left hand in an electric fan and was brought at once to Passavant Memorial Hospital emergency room. There were found numerous lacerations and abrasions (Fig 3, a, b) (1) Laceration over the dorsum of the proximal interphalangeal joint of the index finger with division of the extensor tendon and of the joint capsule (2) Laceration and abrasion over the lateral surface of the middle phalanx of the index finger with loss of one-half square inch of skin. (3) Small lacerations over the volar surface of the proximal interphalangeal joint of the index finger (4) Abrasion with loss of skin over dorsum of the distal phalanx of the middle finger (5) Laceration over the proximal interphalangeal joint of the middle finger (6) Laceration on the dorsum of the middle phalanx of the middle finger (7) Laceration on the volar surface of the proximal interphalangeal joint of the middle finger (8) A laceration at the base of the nail of the ring finger The

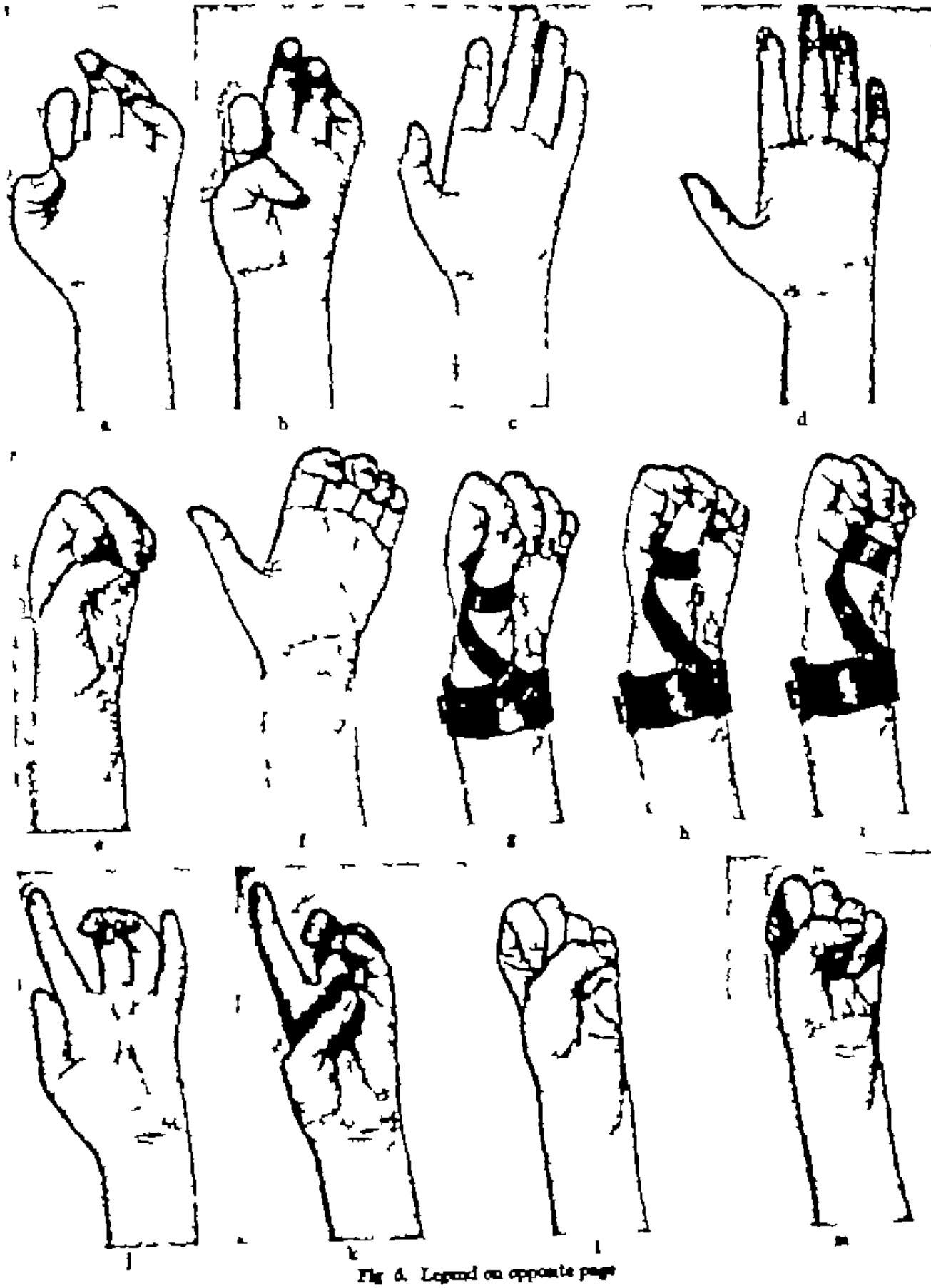

Fig. 6. Legend on opposite page

patient was a mechanic, and although his hands were greasy and black, they were not contaminated with street or garden dirt, and a primary closure was decided upon He was taken immediately to the operating room and anesthetized. The whole hand and then the wounds were thoroughly washed with generous amounts of soap and water, devitalized tissue was excised, and primary repair was performed The joint capsule and the extensor tendon of the index finger were sutured and the skin closed over them Two denuded surfaces, one on the index finger and one on the distal phalanx of the middle finger, were covered with razor grafts, the other lacerations were closed by suture An extension splint and sea sponge pressure dressings were applied The man was discharged on the third day, to return at intervals for dressings Healing occurred *per primam* and the patient returned to full time work 4 weeks later The degree of functional return 6 weeks after operation is shown in Figure 3, c, d, e Subsequent examination has shown further improvement in flexion of the proximal interphalangeal joint of the index finger

The 3 preceding cases illustrate the indications for primary tendon repair All 3 patients were seen almost immediately after injury, and operation was performed within 3 hours In each case a relatively clean object produced the injury, in 1 case, a glass door, in another, a broken piece of glass from a 5 gallon water bottle, and in the third, an electric fan The hands of the patients were relatively clean, although in the case of the third patient, some explanation is necessary This man was a mechanic whose hands were constantly subjected to grease and machine dirt Although at first glance there might be some question as to the advisability of primary suture, it has been our experience that machine shop contamination is not as dangerous as soil or street dirt contamination Such hands are sometimes quite difficult to cleanse, but we have found that they are usually amenable to primary repair

The 4 following reports deal with tendon injuries repaired secondarily, at intervals varying from 11 weeks to 4 years after the injury In 2 instances, no attempt was made at the time of the injury to repair the tendon damage, in 2 instances, incomplete operations were performed

CASE 4 E W, Passavant Memorial Hospital, 19569 (October 2–5, 1934) A housewife 26 years of age sustained a deep cut with a paring knife on the volar surface of the proximal phalanx of the left thumb She treated this herself by the application of an antiseptic and an immobilizing dressing, and healing took place in a few days She was unable to flex the thumb at the metacarpophalangeal joint following this injury (Fig 4, a, b) At operation, 11 weeks later, a complete division of the flexor pollicis longus was found The distal stump had rolled up and retracted to the region of the interphalangeal joint while the proximal stump had pulled upward to the base of the metacarpal, but was prevented from retracting any farther by a well developed mesotenon which was found at the region of the metacarpophalangeal joint. An end-to-end suture was performed and a splint was applied to keep the wrist moderately flexed and the thumb adducted and only slightly flexed The wound healed by primary intention with complete restoration of function (Fig 4, c, d, e)

CASE 5 W V M, Passavant Memorial Hospital, 14075 (May 18–25, 1933) A dentist, aged 38 years, cut the palm of his right hand on a broken porcelain faucet, February 5, 1933 A tourniquet was applied and the man was taken to a hospital where a tendon to the index finger was sutured, and a search was made for the flexor pollicis longus tendon which was not located The skin was sutured and the wound healed by primary union After the wound had healed, he noted loss of sensation of the palmar surface of the thumb, the index finger, and radial half of the middle finger, and loss of flexion of the thumb and index finger At time of examination, 3 months later (Fig 5, a, b, c, d), there was loss of flexion of the interphalangeal joint of the thumb and index finger, and sensory loss over the radial half of the palm, volar surfaces of the thumb and index finger, and radial half of the middle finger The power of rotation of the thumb was absent.

At operation May 19, 1933, the flexor pollicis longus and both flexor tendons of the index finger were found to have been divided The median nerve had been partially divided just at the point where it gives off the common digital branches, and only the branch going to the contiguous borders of the ring and middle fingers was left intact. The ends of the flexor pollicis longus had separated about 2½ inches, but after being released, moved freely in the sheath, and a good approximation was obtained with some difficulty The flexor tendons of the index finger were sutured end-to-end and the lumbrical muscle was laid between them The median nerve was somewhat difficult to suture, since, after excising a neuroma and scar tissue, there were three distal segments to suture to one proximal segment. The incision healed *per primam*, and the condition at the end of 1 month is shown in Figure 5, e, f, g, h, i, j, which show flexion to be returning in the thumb and index finger A strap was applied to produce rotation of the thumb One year later, the index function was 90 per cent normal, the distal phalanx of the thumb could be fully flexed, but could not be completely extended if the metacarpophalangeal joint was extended Rotation was beginning to return to the thumb The area, still anesthetic to cotton, was hyperesthetic to pin prick, so that there was good evidence of sensory return

CASE 6 D H, Passavant Memorial Hospital, 13098 (February 12 to February 19, 1933) This patient, a girl, 16 years, on October 31, 1932, was carrying a jar of tomatoes across the floor when she slipped and fell, broke the jar, and sustained a deep laceration of the left palm. A clean

Fig 6 Case 6 Division of median and ulnar nerves, of flexor digitorum sublimis of index, middle, ring, and little fingers, and of flexor digitorum profundus of the middle, ring, and little fingers Secondary repair 3½ months after injury a, b, c, and d, Before operation. The transverse scar of the injury is seen across the base of the palm The patient cannot flex the middle, ring, and little fingers at the interphalangeal joints, cannot abduct and adduct the fingers, and cannot rotate the thumb or oppose the thumb and little finger e, f, g, h, and i, Two months after operation The fingers can be flexed, but cannot as yet be completely extended A wrist strap and thumb loop have been applied to rotate the thumb and relax the thenar muscles j, k, l, and m, were taken 6 months after operation It will be noted that the fingers can be completely flexed, though they can not as yet be completely extended The fingers can be slightly abducted and rotation of the thumb is returning

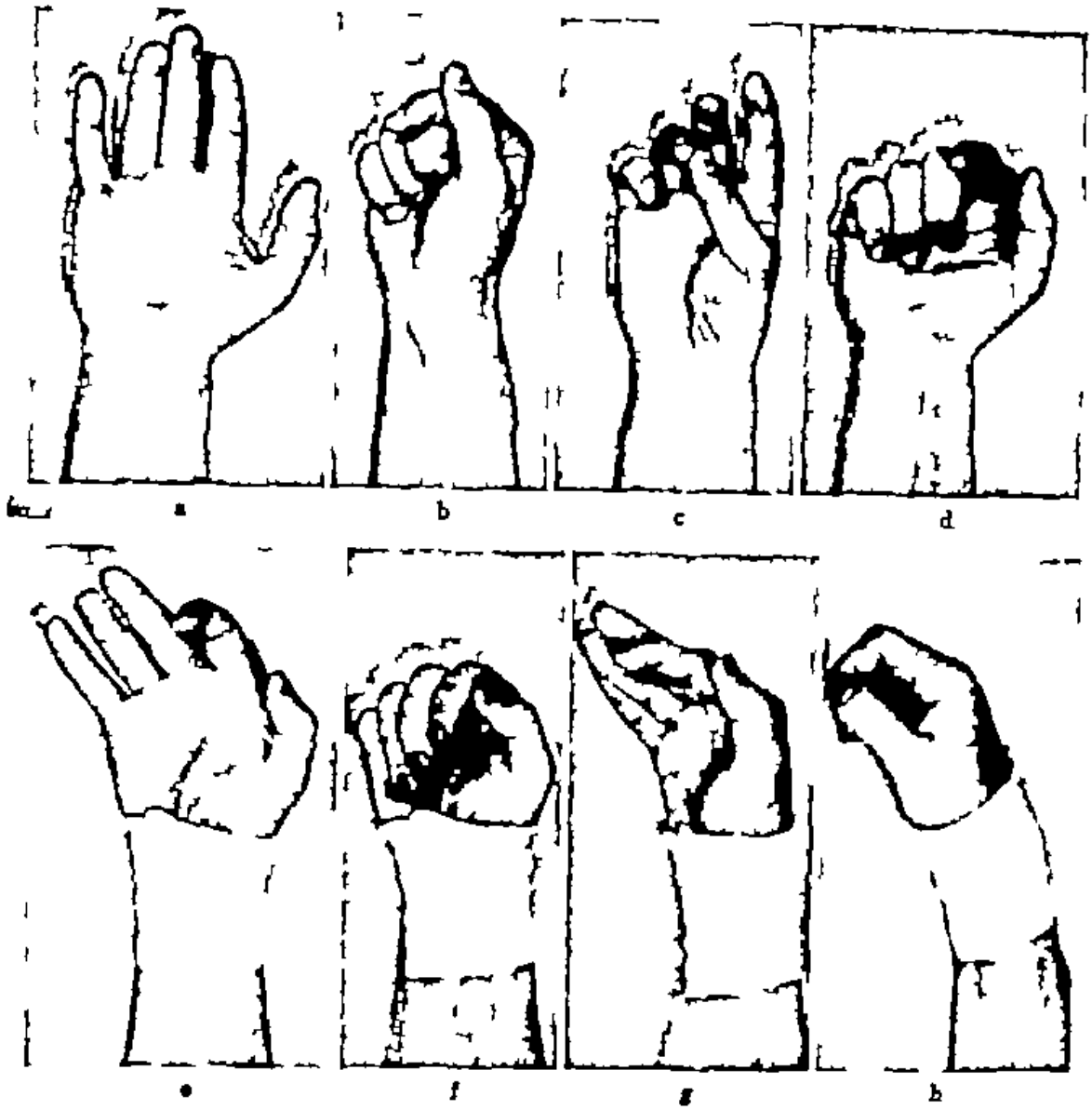

Fig 7 Case 7 Division of median nerve, flexor pollicis longus, flexor digitorum profundus of index finger and flexor digitorum sublimis of all four fingers on a broken porcelain faucet 4 years previously The good rotational function of the thumb is difficult to explain since complete median nerve division with a large proximal neuroma was found t operation a, b, c, and d, Condition of the hand before operation 4 years after injury e, f g, and h, One month after operation shows returning flexion power in index finger and thumb

bath towel was wrapped tightly about the hand and the wound was sutured by physician The wound healed within 6 weeks; the only complication being a single stitch abscess

Examination of the hand 3½ months later February 9 1933 (Fig 6 a, b, c, d), revealed inability to rotate or oppose the thumb and little finger; inability to flex the metacarpophalangeal joints of the middle, ring, and little fingers; disturbed flexion of the proximal interphalangeal joints of these fingers, inability to abduct and adduct the fingers, inability in extension of the distal interphalangeal joint of the index finger loss of abduction and adduction of the fingers and atrophy of the thenar and hypothenar eminences There was a well healed transverse scar across the proximal end of the palm extending from the base of the hypothenar eminence laterally and slightly proximalward to the region of the carpometacarpal joint of the thumb There was practically complete sensory loss over the palm except for narrow strip on the extreme radial side and loss over the volar surface of the little, ring, and middle fingers and ulnar one half of the index finger There was also sensory loss over the dorsum of the terminal phalanges of the index, middle, ring, and little fingers

At operation February 3, 1933, there was found division of the median and ulnar nerves, the flexor profundus tendons of the little, ring, and middle fingers and sublimis tendons to the index, middle, ring, and little fingers The distal segments of the flexor profundus tendons of the middle, ring, and little fingers were sutured en masse to their proximal stumps The sublimis tendons of the index and middle fingers were sutured separately to their respective stumps, while the sublimis tendons of the ring and little fingers were sutured as one The median and ulnar nerves were sutured end-to-end with fine silk A flexion splint and a pressure dressing were applied.

The wound healed *per primam* and physical therapy was started early Two months after operation, flexion had improved considerably and a wrist strap and thumb band had been applied to rotate the thumb and relax the thenar muscles (Fig 6, e, f, g, h, i)

Six months after operation, the function of the hand was excellent. The patient was regaining power of rotation of the thumb, the thenar and hypothenar atrophy was disappearing, and except for some trouble in extending the three medial fingers, her hand was quite useful. Sensory examination at this time showed beginning return of response to pin prick over the proximal three-fourths of the palm

CASE 7 F B McA, Passavant Memorial Hospital, 14268 (June 6–13, 1932) In the spring of 1929 the patient, a man 26 years of age, sustained a deep laceration of the palm of the right hand, when a porcelain faucet handle broke while he was trying to turn off a shower The wound was covered with a towel and the patient was taken to a hospital where an operation was performed, at which time the tendons of the index finger and thumb were sutured and the wound was closed Since the accident, he has been unable completely to flex the index finger and thumb, and there has been marked sensory impairment of the palm

Upon examination 4 years later (June, 1933) there was found a puckered transverse scar in the palm over the region of the transverse carpal ligament, there was sensory impairment to light touch and pain over the area of distribution of the median nerve, and impaired flexion of the interphalangeal joints of the thumb and index finger A diagnosis was made of median nerve division and division of the flexor tendons of the thumb and index finger The only incompatible feature in the picture was the lack of impairment of rotation of the thumb (Fig 7, a, b, c, d)

At operation there was found division of all the sublimis tendons, of the flexor profundus of the index finger, of the flexor pollicis longus, and of the median nerve The proximal segments of the divided tendons had retracted 1½ to 2 inches above the wrist. The proximal and distal segments of the median nerve were located the distal segment at the level of the outstretched thumb, the proximal, in the carpal tunnel Although there was no question as to complete division of the median nerve, the thenar muscles showed remarkably good nutrition and not at all the picture typically present after median nerve division. After careful freeing of the divided structures, the profundus tendon of the index finger and the flexor pollicis longus were united by end-to-end suture, the sublimis flexors were repaired, the neuroma was excised from the median nerve, and end-to-end suture performed The deep palmar scar and fibrotic remains of the transverse carpal ligament were excised, the wound was closed, and a pressure dressing and dorsal splint were applied The wound healed nicely and the beginning functional return 1 month after operation is shown in Figure 7, e, f, g, h.

TANNIC ACID AND SILVER NITRATE IN BURNS[1]

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THE application of a new treatment for burns has brought about a new conception of them (1) A burn lesion is not the burn alone but it is the burn plus all those events which develop because the treatment does not check them. The treatment here presented goes far toward controlling all such developments in fact, the tannic acid-silver nitrate treatment changes the burn lesion into almost a surgical wound

The treatment of a serious burn is carried out as follows The patient is given a narcotic which is repeated as often as may be necessary for comfort. Fluids must be forced throughout (2) Grease or oil in any form should not have been used If such an application unfortunately has been made it must be removed with ether or benzine before treatment is applied. All blebs are to be opened and all loose skin and other burned tissue are to be removed. A thorough application of fresh 5 per cent tannic acid solution is made by means of cotton swabs Following this, 10 per cent silver nitrate solution is applied in the same manner When this second solution is put on, a protective coagulum forms at once Thus, a task that formerly required up to 24 hours is accomplished in a few minutes The patient is placed in a tent heated by electric light bulbs and the areas treated are dried and kept dry Drying the coagulum and keeping it dry is of the utmost importance In a few days the coagulum begins to loosen and is removed as early as possible When the crusts come away large areas and not infrequently all, of the burned surfaces will be found to be entirely healed Occasionally moisture will be hidden beneath crusts where drying has not been accomplished satisfactorily and such areas are unhealed when the crusts come away Where the coagulum is adherent but loose, it is removed, a scalpel being used if necessary Unhealed areas are treated by the application of oxyquinoline sulphate scarlet R gauze (3) the formula of which is

R. Oxyquinoline sulphate	grains	15
Chlorbutanol (chlorotone)	grains	40
Scarlet R ointment, 5 per cent	ounces	4
Liquid petrolatum	drams	4

A softer ointment may be made by replacing the petrolatum in the scarlet R ointment by oleum ricini. From these ingredients an ointment is made which is heated on a water bath and into which wide mesh rolled gauze bandages are immersed The warp and woof are impregnated but the mesh is open. This gauze is applied to the unhealed areas in a single layer over which a light pad of dry gauze is placed. Healing is greatly speeded up. This gauze has a wide range of usage in the healing of wounds of all kinds.

The schedule here outlined—the avoidance of grease and oil, the giving of a narcotic, the application of tannic acid followed by silver nitrate drying the coagulum keeping it dry and removing it early forcing fluids and the stimulation of epithelization—constitutes a superior method of treating serious burns and results in the saving of lives and the minimum of scars and contractures Under this treatment skin grafting and other secondary corrective measures are very greatly reduced

The most important result of this treatment is the saving of lives that would be sacrificed by a slower method the patient too is very comfortable throughout the shortened course of treatment Greases and oils have served their time and now should be placed in the burn museum among

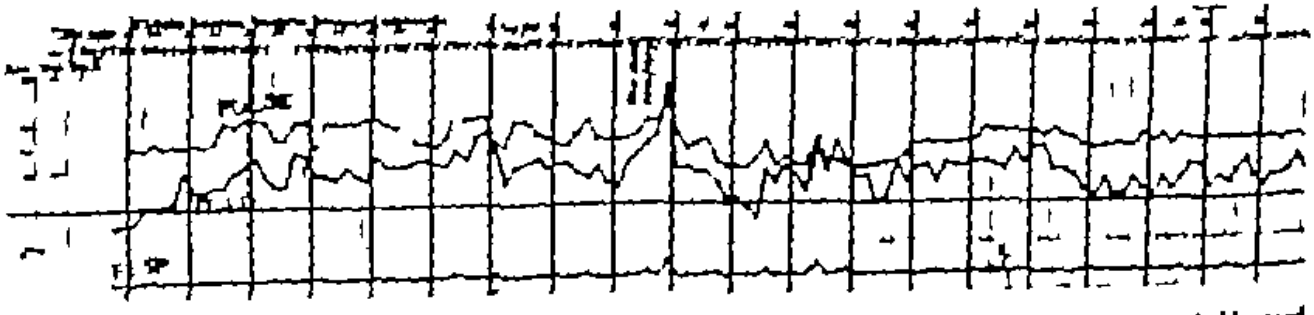

Fig Case 1 Temperature above 101 degrees only twice pulse never above 118 Condition remarkably good throughout (Continued on next page)

[1]Presented at the Symposium on Industrial Medicine and Traumatic Surgery before the Clinical Congress of the American College of Surgeons, San Francisco, October 31-November 4, 1935

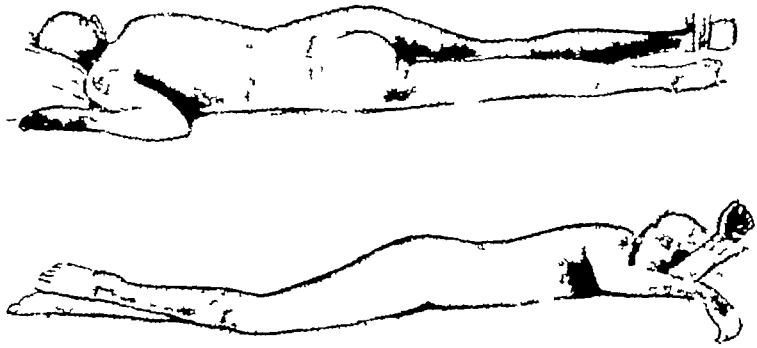

Fig 2 Case 1 above, R B Fifty four per cent gasoline burn Treated with tannic acid and silver nitrate 4 hours after burned Drawing from sectional photo graph taken on fourth day, showing back and left side
Fig 3 Case 1 Same as seen from the right front

other antiquities of medicine Tannic acid alone (4) tans the surface in from 12 to 24 hours, and a further period is necessary that the area may become dry Tannic acid solution followed by silver nitrate leatherizes the surface at once, and it is quickly and easily dried and kept dry The surface becomes tanned and dry in minutes instead of hours The rapid formation of coagulum, through the rapidity alone saves lives

When grease has been applied and/or the areas are not kept dry, the progress of the patient is not as favorable as here outlined The temperature, pulse, and blood counts go slightly higher and there may be traces of albumin in the urine The nearer the outlined schedule is adhered to, the better will be the results The treatment is best carried out in a small room rather than in a large room or ward

The loss of body fluids is stopped at once by the prompt sealing of the oozing surfaces A prolonged concentration of body fluids is inimical to life The early formation of the coagulum supplies a barrier through which the loss of body fluids cannot and does not take place Shock is immediately and definitely minimized by this treatment, and patients pass through what otherwise would be the period of initial shock, in good condition Thus they avoid the first critical period of their burn Not infrequently, 24 hours after a severe burn, instead of being in shock, the patient wishes to go home or to carry on his business from his bed

Under past treatment of burns there is an absorption of substances which affect the kidneys, liver, spleen, adrenals, and other internal organs Such effects have not been noted in patients treated primarily by tannic acid and silver nitrate, in the absence of grease Urinary suppression, albumin, and other abnormal elements, except sugar in the early specimens, have not been found Thus this hazard is minimized

When moisture is applied to a wound over a period of hours, infection develops and the tissues become edematous with some further breaking down In the few minutes required for the application of the tannic acid and silver nitrate solu-

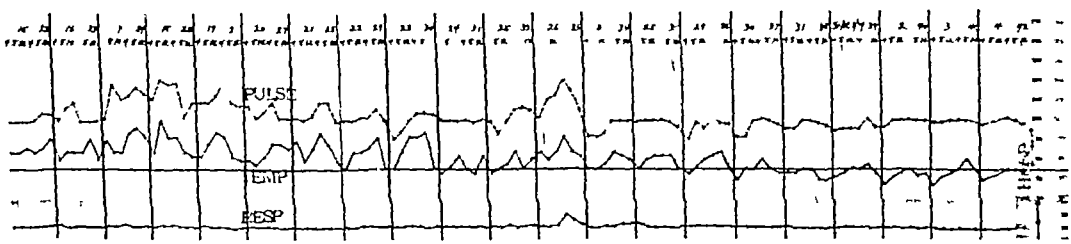

Fig 1 Case 1 (Continued from facing page.)

TABLE I—CASE R B DETAILS OF CONDITION THROUGHOUT THE 42 DAYS UNTIL HEALING WAS COMPLETE

Date 1924		Fluid intake	Urine	Hemoglobin %	Red blood cells millions	Leucocytes	Small lymphocytes	Large lymphocytes	Tissue fluids	Polymorphonuclear neutrophiles	Eosinophiles	Others	Total cells
July	5 pm	6pm		104	4 55								
	26 am pm	[illegible] 3[illegible]	3[illegible]	32	4 4 30	1[illegible]				79			
	27 am pm	3760 3760	3[illegible] 7[illegible]	103	66	6[illegible]	42			87			
	28 am pm	[illegible] 3 [illegible]	1[illegible] 7[illegible]	8[illegible] 3	4 4 [illegible]	[illegible]	4			77			6
	29 am pm	7[illegible] 8[illegible]	[illegible] 7[illegible]	10 104	3 [illegible] 3 4	6[illegible]	30			79			32
	30 am pm	1[illegible] [illegible]	7[illegible] 8[illegible]	4 100	3 3 [illegible]	6[illegible]	30			69			30
	31 am pm	3 [illegible] 1[illegible]	8[illegible] 7[illegible]	10 11	4 [illegible] 3 [illegible]	8[illegible]	30			64	4		37
August		1[illegible] [illegible]	[illegible] 1[illegible]	10 100	6[illegible] 43	9[illegible]	71	5		79			[illegible]
		[illegible] [illegible]	[illegible] 11[illegible]	107	3 [illegible]	[illegible]	7			8[illegible]			
	1 am pm	[illegible] [illegible]	1[illegible] 1[illegible]	[illegible]	[illegible]	17[illegible]	[illegible]			73	4		
		[illegible] [illegible]	7[illegible] 8[illegible]	7	7[illegible]	[illegible]	7			8[illegible]			[illegible]
	5 am pm	[illegible] [illegible]	1[illegible] 1[illegible]	104	6[illegible]	[illegible]	17			8[illegible]			
	6 am pm	[illegible] [illegible]	1[illegible] 3[illegible]	[illegible]	6[illegible]	16[illegible]	34	3		71	1		1
	7 am pm	[illegible] [illegible]	1[illegible] 1[illegible]	106	6[illegible]	1[illegible]	3			8[illegible]			3
	8 am pm	1[illegible] [illegible]	1[illegible] 7[illegible]	[illegible]	5 5	[illegible]	14			8[illegible]			17
	9 am pm	[illegible] [illegible]	[illegible] 1[illegible]	[illegible]	[illegible]	[illegible]	[illegible]			77			7
	10 am pm	1[illegible] 1[illegible]	1[illegible] 1[illegible]	105	5 [illegible]	18[illegible]	18			78			12
	11 am pm	[illegible] [illegible]	7[illegible] 5[illegible]	103	[illegible]	[illegible]	[illegible]			77			
	12 am pm	[illegible] [illegible]	1[illegible] 8[illegible]	[illegible]	7	1,1[illegible]	17			8[illegible]			[illegible]
	1 am pm	[illegible] [illegible]	1[illegible] 1[illegible]	108	4 47	[illegible]	[illegible]			8[illegible]			[illegible]
		[illegible] [illegible]	[illegible] [illegible]	[illegible]	4 [illegible]	[illegible]	[illegible]			7			
	3 am pm	[illegible] [illegible]	[illegible] [illegible]	[illegible]	[illegible]	1[illegible]	33		3	68			
	14 am pm	[illegible] [illegible]	1[illegible] [illegible]	[illegible]	4 [illegible]	1[illegible]	[illegible]	2		4	3		11
	7 am pm	[illegible] [illegible]	[illegible] [illegible]	10	[illegible]	[illegible]	34			6[illegible]			
	15 am pm	[illegible] [illegible]	[illegible] [illegible]	105	4 [illegible]	[illegible]	[illegible]		2	66			
	16 am pm	[illegible] [illegible]	[illegible] [illegible]	97	33	[illegible]	35			6[illegible]			
	17 am pm	[illegible] [illegible]	[illegible] [illegible]	[illegible]	33	[illegible]	[illegible]			6[illegible]	3		
		[illegible] [illegible]	[illegible] [illegible]	105	33	[illegible]	[illegible]			13			
		[illegible] [illegible]	[illegible] [illegible]	[illegible]	33	[illegible]	3			6[illegible]			

TABLE I—CASE I K B DETAILS OF CONDITION THROUGHOUT THE 42 DAYS UNTIL HEALING WAS COMPLETE Continued

Date 1934		Fluid intake	Urine	Hemoglobin %	Red blood cells, millions	Leucocytes	Small lymphocytes	Large lymphocytes	Transitionals	Polymorphonuclear neutrophiles	Eosinophiles	Others	Staff cells
August	23 am	1920	700	100	4 19	8150	35			62	3		
	pm	1590	660										
	24 am	1660	850	96	4 00	8 00	35			61	3		
	pm	1980	940										
	25 am	2190	1250	96	4 41	8500	8	1		67	4		1
	pm	1890	1440										
	26 am	1650	850										
	pm	2010	1080										
	27 am	1560	900	100	4 36	8750	36			61	2		3
	pm	1470	1020										
	28 am	1440	1350										
	pm	1200	1000										
	29 am	1300	1100	110	4 43	12950	36	1		63			3
	pm	1530	840										
	30 am	1560	1300										
	pm	1600	1000										
	31 am	1700	1200	111	4 60	10150	37			59	3	1	1
	pm	1590	540										
Sept	1 am	1320	1100										
	pm	1500	900										
	2 am	1400	1350	110	4 64	13350	37			60	2	1	
	pm	1590	770										
	3 am	1000	500										
	pm	1590	400										
	4 am	1000	600	107	4 45	9 00	46			51	3		
	pm	1500	700										

tions, the tissues do not have time to absorb moisture and become water-logged, therefore, they dry quickly and do not break down

Instead of the usual blood concentration, we find that the hemoglobin and red cell count returns early to normal The white blood cell count is low, the staff cells being relatively few throughout the entire healing period The temperature and pulse rate are surprisingly low at all times, and the organisms of infection do not develop Moisture taken from beneath intact coagulum has shown no bacterial growth, while that from broken areas showed Staphylococcus albus

When extremities are involved, they should be placed in slings within the tent to allow the circulation of warm air entirely around them, thus keeping the coagulum dry on all surfaces Many patients with less extensive burns who usually require hospitalization are ambulatory with this treatment, and not a few are seen by the surgeon only once or twice Dressings of any kind are not required, the patient being admonished to keep the treated areas dry

The second critical period, that of infection, is also conspicuous by its absence, because there is little or no moisture or infection beneath the coagulum, as all surfaces are commonly completely healed when it comes away No cause, therefore, exists for a secondary temperature rise on the sixth or eighth day The treatment provides an antiseptic covering for the burned areas and one that is insoluble and not absorbable Coagulum formed by the application of tannic acid followed by silver nitrate is thin and flexible and allows motion, especially turning

The frequent disturbing of the patient by the applications of the slower method of tanning is avoided, the nurse s major problems are the administration of fluids and the keeping of the coagulum dry Further local applications are not necessary except to those few blebs which ordinarily make their appearance on the second day Intravenous and rectal fluids are required for only a short period, as the mouth intake early assumes large proportions under the urgings of a diplomatic nurse At least 1000 cubic centimeters for every 25 pounds body weight, every 24 hours should be administered The necessity of administering salt must not be overlooked

The repeated applications of medication which rapidly become cold and wet the bedding, add to

Fig 4 Fig 5 Fig 6

Fig 4 Case 1 Condition when healing was complete Back of hand and forearm were covered with Thiersch grafts on the twenty-sixth day All other skin surfaces healed smoothly without contracting scars or disfigurement

Fig 5 Case Back and thighs, after healing had been completed The skin is soft and flexible.

Fig 6. Case 1 Showing right leg and thigh healed without hypertrophied scar, contractures or disfigurement Patient left hospital, all healed, on the forty second day

the shock at a time that heat is needed. The brief application of these two solutions does not cause chilling, and the bedding once changed, is there after dry It is necessary to open only the head of the tent to give fluids.

The treatment of burns with tannic acid and silver nitrate speeds up healing and shortens the period of hospitalization very greatly A number of patients with extensive second and third degree burns have completely recovered by the eleventh, twelfth, and thirteenth days many by the twenty-first, and a 54 per cent burn, on the forty-second day In every case in which tannic acid and silver nitrate have been used as a primary treatment, the scarring has been minimum The healed surface is soft and flexible and is covered by a good thickness of epithelium with little scarring The speedy healing makes necessary a lesser amount of skin grafting or other reconstructive surgery not that skin grafting or other secondary procedures are entirely unnecessary but they are very greatly minimized.

Fig 7 Case 2.

The silver nitrate solution is apparently completely combined with the tannic acid in the surface fluids and is fixed in such a manner that no absorption takes place for in no case in which this treatment has been applied has there been any evidence of argyria. The only patient who has died following the use of this treatment was a 77 year old man with an 80 per cent burn.

When tissue is destroyed by the direct action of the burning agent and when the primary destruction removes all epithelial islands including those of deep glands, then skin grafting or other reconstruction procedures must be done and the operation had best be done early Under treatment by tannic acid and silver nitrate if grease has not been previously applied, there is no further breaking down of tissue, the epithelium quickly grows out over the burned area under the dry coagulum, and healing is accomplished with minimum scars and contractures. Details of

nursing must be carried out with this treatment as with tannic acid alone

The tannic acid and silver nitrate treatment has been used by the author approximately 16 years for the removal of tattooing It was first used for the treatment of burns about 2 years ago following a burn on his own arm The result was so superior that he was encouraged to use it on patients with small burns Finally the treatment proved itself by successfully healing a 54 per cent burn and the patient left the hospital on the forty-second day Tannic acid and silver nitrate has been found valuable also in the treatment of superficial injuries, which it seals, preventing infection It is of value too in the treatment of bed sores

ADVANTAGES

Sixteen points of the superiority of tannic acid and silver nitrate treatment applied in burns are worth consideration

1 The saving of lives that would be lost through the slower method of tanning

2 The immediate stopping of the loss of body fluids, thereby preventing the consequent concentration of the blood

3 The immediate prevention or very definite minimizing of shock

4 The immediate prevention of the absorption of toxic products

5 The prevention of infection by the short period of application of moisture and the early drying of the tanned tissues

6 The saving of the kidneys and other organs from the effects of fluid concentration and the absorption of toxins and infection

7 The greater comfort of the patient

8 The fact that the patient is safely carried past the first 24 hours, the most critical period following a serious burn

9 The fact that the patient avoids the second critical period, that of infection and late absorption of toxic products

10 The simplification of the nursing problem, especially in the first 24 hours

11 The prevention of further breaking down of tissues, resulting from long application of wet dressings

12 The prevention of chilling, resulting from the long application of cold, wet dressings

13 The formation of a thin, flexible coagulum

14 The speedy healing of the burned areas with a shortened period of hospitalization

15 The prevention or minimizing of heavy contracting scars by early rapid healing in the absence of infection

16 The lessening of the amount of skin grafting and secondary corrective surgery

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SILICOSIS AND ITS CONTROL[1]

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IT is the purpose of this article to discuss silicosis, briefly outlining salient facts relative to its etiology clinical manifestations, complications, diagnosis, and prevention. Our remarks are limited to that diseased condition due to prolonged exposure to atmospheres containing free silica. The Committee on Pneumoconiosis of the Industrial Hygiene Section of the American Public Health Association (38) gives the following definition

> Silicosis is a disease due to breathing air containing silica (SiO_2) characterized anatomically by generalized fibrotic changes and the development of miliary nodulation in both lungs, and clinically by shortness of breath, decreased chest expansion, lessened capacity for work, absence of fever increased susceptibility to tuberculosis (some or all of which symptoms may be present), and by characteristic X-ray finding

A certain amount of general information relative to the pathology resulting from the inhalation of dusts has been in existence since the time of Hippocrates (430 B C.) Some of the early writers discussed such diseases of the lung under the general term, pneumoconiosis. Professor Collis (6) in his 1915 Milroy lectures, furnished us with an excellent historical review of the subject of the industrial pneumoconioses. Rovida in 1871 used the term silicosis in reporting a case of pneumoconiosis, in which he determined, by chemical examination of the lungs, that the condition was due to silica.

Although other dusts, when inhaled in sufficient concentrations over a long enough period of time, have been shown capable of producing a definite pulmonary fibrosis, nevertheless, the pneumoconiosis characterized by nodular fibrosis has to date been shown, clinically and experimentally to be associated only with the inhalation of dusts containing silica. It has been established that exposure to dusts consisting wholly of free silica (quartz) produces this disease, this has not been shown to be the case for any dust not containing free silica.

Silicosis has been reported in the medical literature from practically all civilized countries. Being an occupational disease, it occurs only in adults, and its distribution among them is limited to those engaged in occupations requiring the use or processing of siliceous materials.

Silica is the most abundant constituent of the minerals and rocks that make up the earth's crust. It occurs in two forms, free and combined. The free silicas as a group are definite compounds in the form of SiO_2. The combined forms are spoken of as silicates. The three most important free silicas are quartz, opal, and flint.

OCCUPATIONAL EXPOSURE TO SILICA

Owing to the fact that the earth's crust contains so great an amount of silica, it is obvious that those occupations concerned with the driving of tunnels, development of highways, and mining, are frequently associated with a silicosis hazard. A second class of occupations exposing the workers to this hazard are those connected with industries having to do with the processing and industrial use of mineral products, such as, the smelting and refining of ores the use of sand and gravel for structural purposes, the carving of stone, particularly granite the manufacture and use of silica-containing abrasives, and the processing of the various forms of free silica.

Lanza and Vane (21) in their discussion concerning the prevalence and effect of silicosis, state, "Our very rough, but obviously conservative estimate of the number of workers exposed to silica dust to a harmful degree in the United States is, therefore, upward of 500,000."

FACTORS INFLUENCING THE ACTION OF SILICA DUST PARTICLES AS THE EXCITING CAUSE OF SILICOSIS

Although it has been accepted that silica is the exciting cause of silicosis, there are certain factors which must be considered as influencing its action

Early workers were inclined to consider that the injury produced by the dust particle was due to mechanical irritation produced by its hard and cutting edges Gardner (9) has shown experimentally that the inhalation of finely divided carborundum dust, of a greater hardness than silica particles, does not produce the nodular reaction characteristic of silicosis. Collis (7) was one of the early workers to draw our attention to the chemical action of dust. Gye and Kettle have shown that silica in solution or non-crystalline form, exerts a toxic action upon the tissues which leads to the proliferation of fibroblastic cells. Lately Miller and Sayers have reported results of experimental studies which illustrate clearly the

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TABLE I—SIZE-FREQUENCY DISTRIBUTION OF VARIOUS INDUSTRIAL DUSTS AS COMPARED TO OUTDOOR DUST

Kind of dust	Number of samples	Median	Average frequency in per cent—Size group in microns											
			0 to 0 49	0 5 to 0 99	1 0 to 1 49	1 5 to 1 99	2 0 to 2 49	2 5 to 2 99	3 0 to 3 49	3 5 to 3 99	4 0 to 4 49	4 5 to 4 99	5 0 to 5 49	5 5 to 5 99
Outdoor dust	179	0 5	56 0	41 0	2 5	0 5								
Sandblasting	9	1 4	1 4	19 7	34 7	20 3	12 6	5 2	2 8	1 6	1 1	0 2	0 2	0 2
Granite cutting	4	1 4	2 0	19 0	33 6	24 5	10 4	4 6	3 1	6	9	3	1 0	
Trap rock milling Crusher house	1	1 4		13 0	39 0	33 0	10 5	2 5	2 0					
Screen house	1	1 3	2 0	31 5	33 0	16 0	10 0	4 5	2 5	5				
Disk crusher	1	9	10 0	48 0	31 0	6 0	3 0	1 0	1 0					
Foundry parting compound	2	1 4	0 5	27 0	42 0	17 3	9 2	5 0	1 5	2 0	5			
General foundry air	1	1 2		26 0	48 0	17 0	8 0	1 0						
Talc milling	1	1 5		16 0	32 0	20 0	13 0	7 0	5 0	2 0	2 0	2 0		1 0
Slate milling	1	1 7	1 0	13 0	29 0	17 0	14 0	14 0	6 0	4 0	1 0		1 0	
Marble cutting	1	1 5		12 0	37 0	21 0	10 0	11 0	3 0		1 0	2 0	2 0	1 0
Soapstone dust	2	2 4	1 2	16 0	19 0	13 0	11 0	6 0	6 5	4 5	5 5	3 3	2 5	11 5
Aluminum dust	1	2	3 0	8 0	20 5	14 0	11 5	9 0	6 5	3 0	3 5	4 0	7 0	10 0
Bronze dust	1	1 5	1 0	12 0	33 5	25 0	21 0	6 0	1 5					

reaction of peritoneal tissues to certain dusts Only the silica containing dusts have uniformly produced a proliferative reaction Other dusts have been either completely absorbed, leaving no scar tissue, or have remained unaltered in the form in which they were injected These latter reactions are classed as absorptive or inert

Since dust, to exert its harmful action, must enter the finer divisions of the lung, the particle size of the atmospheric dust bears a definite relationship to the injurious effect produced The silica must be present in the air, in particles small enough to enter the finer air spaces and of such dimensions that the phagocytic cells may engulf them From our knowledge of these cells, we know that they usually are unable to handle bodies greater than 10 microns in their greatest dimensions The natural defenses of the respiratory tract probably prevent many particles larger than 10 microns ever reaching the finer divisions of the lung, and such as do are likely to be expelled with the bronchial secretions The soluble silica plays a definite part in the production of the disease, and the size of the particle also affects the rate of solution, due to the fact that the smaller the particles, the greater the total surface area exposed to the action of solvents

Table I shows the size-distribution of various industrial dusts as compared with the dust particles observed in the outdoor air in the general atmosphere It is found that about 70 per cent of the particles found in industrial dusts generally are between 0 5 and 3 microns in diameter There are, no doubt, many times as many particles too small to count by the method used, but experimentally it has been shown that a great percentage of such submicroscopic particles are not retained in the lungs but pass out with the expired air Sayers (31) has shown that less than 15 per cent is retained when the finer particulate matter, such as lead in the form of fumes, is inhaled The greater majority of particles found upon microscopic examination of the lung also fall within the limits of from 1 to 3 microns

Another reason for considering the size of the particles as affecting the harmfulness of the dust is that it is the larger ones that settle out rapidly, while the rate of falling for the smaller particles is very slow Figure 1 illustrates graphically this difference those under 1 micron fall at a rate of from 1 to 3 feet per hour, varying with the specific gravity, while a particle 5 microns in diameter of 7 specific gravity falls about 60 feet per hour Particles of more than 10 microns would settle out in a relatively short time The fact that the finer particles remain suspended in the atmosphere for long periods greatly increases their chance of being inhaled

Thus we may say, from the viewpoint of etiology, that the harmfulness of a given dust is directly influenced by the number of particles it contains of free silica less than 10 microns in

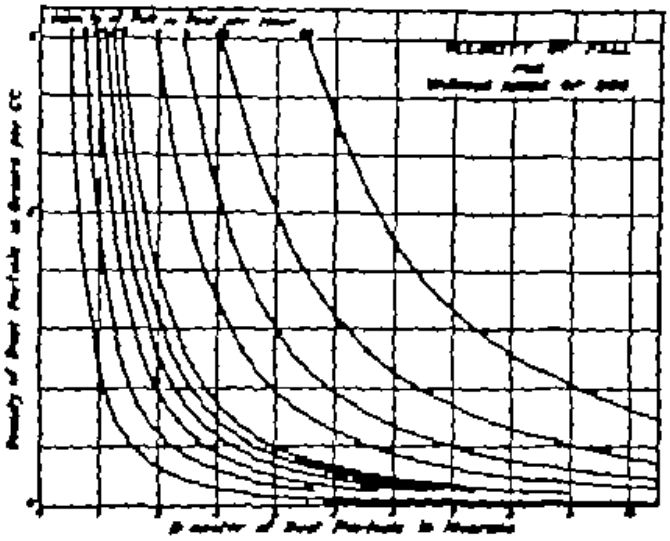

Fig 1 Velocity of fall for various kinds of dust

diameter and probably the greatest harm is produced by those between 1 and 3 microns.

The relationship of dust concentration and of the duration of exposure is closely associated in its etiological significance. The rate at which silicosis will develop, excluding certain factors considered as predisposing, depends upon the dosage of free silica. This dosage is obviously dependent upon the amount of silica in the air inhaled and the duration of exposure

In 1902 a committee of which Dr J S Haldane was a member reported upon an investigation made to determine the cause of excessive mortality rates from tuberculosis among the Cornish tin miners. This group decided that it was evident that the inhalation of stone dust by these men in the performance of their tasks as miners, was the cause of permanent damage produced upon the lungs Furthermore, they noted that the condition developed gradually in the case of the ordinary miner but rapidly in the case of the machine workers who were exposed to greater amounts of dust. Dr Watkins-Pitchford and Dr *Mavrogordato and other* South African workers, in their discussions relating to the etiology of silicosis, emphasize the relationship of the concentration of dust and duration of exposure to the degree of lung changes produced Mavrogordato has suggested the advisability of intermittent employment as an aid in lessening the amount of changes produced, but aside from the fact that it does delay the reactions, it has not been shown that it could safely be relied on to prevent silicosis, *where exposure is to sufficient* concentrations It is intimated that the rest interval allowed by intermittent employment permits the lung to free itself of some of the particles. This avenue of elimination will vary with the types of dust for example, limestone and coal dust are more readily eliminated than those *concentrations with high percentages of free* silica. Once the dust is taken up by the cell, the direction of the dust cell in its expulsion from the immediate site of action is toward the lymphatics as well as toward the epithelial lining of the bronchioles, and some portion will be retained This rest interval may permit the subsidence of the primary reaction which accompanies the inhalation of foreign particles into the finer lung passages Workers in this country have also shown the relationship of dosage to the severity of the reaction. Reports of the Picher Clinic (32), at the Tri-State District of Oklahoma, Kansas and *Missouri lead and zinc mines*, which is a cooperative undertaking by agents of the operators, the Metropolitan Life Insurance Company the Bureau of Mines, and the Public Health Service, have shown clearly the effects of various periods of exposure to silica as met with in the mining processes carried out in the district. Similar studies upon the health of granite workers (1 30) likewise stress the duration of exposure necessary to produce definite degrees of silicosis.

Some have thought that the relative absence of silicosis in the cement industry was due to the calcium present. However investigations (36) *have led to the belief that the absence of evidence* of extensive pulmonary fibrosis among employees in the cement industry is due to the fact that there is insufficient total exposure to free silica, considering concentration of dust and duration of exposure.

No complete reports of pulmonary fibrosis resulting from the inhalation of organic dusts have appeared in the literature Always when such fibrosis is associated with the breathing of air containing organic dust, *either inorganic dust has* been shown to be present or at least its absence not definitely proved.

In regard to the presence of other irritating dusts, Chapman, Kessler MacDonald, Kilgore, and others have reported cases of so called acute silicosis, resulting from the inhalation of air containing high concentrations of silica, along with strong alkali in a fine powdered form Some have suggested that the rapid action of the silica in the production of pulmonary fibrosis is *aided by the* presence of these alkalis, because silica is more soluble in alkaline solutions Kettle (18) failed to *demonstrate such actions experimentally* and stated that proof is still lacking that any action of the kind may occur Pathological reports furnish evidence of a definite fibrosis, but the

entire picture differs remarkably from that of the typical silicotic, such as has been furnished by Gardner (10) in his reports upon the examination of tissues from clinical cases of silicosis, as well as his pathological reports made from tissues obtained in his experimental studies

Sayers, Meriwether, and Lanza (32) reported that of the employees in the lead and zinc mines, those who gave a history of previous coal mining experience developed a definite silicosis in a shorter time than employees of the same age without this experience This cannot be taken to mean, however, that the inhalation of coal dust hastened the action of silica, for it is doubtful if any of these coal miners had worked where they were not exposed to some free silica, so the total dosage of silica was not the same in the two groups

PREDISPOSING FACTORS AND COMPLICATIONS

Since the literature of practically all the principal nations of the world contains articles on this subject, it is apparent that no nationality is exempt that all races are susceptible, is shown by the wide distribution of silicosis Although the data show that the incidence is higher among the younger miners in districts where the percentage of free silica is high, and among older miners where the percentage of silica is low, age in itself probably is no great factor

Previous occupation of the men may have a definite influence in predisposing to silicosis, if they have been exposed to dust or to other respiratory irritants

Since respiratory infection has been shown to be the greatest predisposing and complicating factor in the development of silicosis, certainly the history of present and past respiratory infections will have to be given consideration in the statistical analysis of records upon which such conclusions are based

The factor of individual susceptibility is often mentioned Generally speaking, if there be any difference in individual susceptibility, it can usually be considered an acquired, not a congenital, condition Ickert quotes Bohme and Lucanus and Schulte-Tiggs as stating that it is essential that the individual possess excellent functioning nasal passageways, in order that the self cleansing mechanism may work efficiently He calls attention to the fact that Irvine, Simpson, and Strachau report the "classical" type of silicosis to be more common among the robust type of individuals with less respiratory reserve Ickert found some slight variation in the susceptibility of persons according to their type of body build As a whole the group classed as slender individuals developed simple silicosis somewhat slower than the stoutly built persons, but the incidence of advanced silicosis was greater in the former class, being nearly double that developing in the sturdy workers

Lehmann's experiments to determine the functional efficiency of the upper respiratory tract in the removal of dust, suggests that abnormalities of the nasal passageways probably play some part in the rapidity with which silicosis may develop Using dust with a high silica percentage, he found that from 8 3 to 73 7 per cent of the dust was retained during passage of air through the nose In carrying out this experiment upon 62 miners, he found that the average retention by the nose in the cases of non-silicotics was about 50 per cent, while in the case of miners with silicosis, the average retention was only about 22 per cent

Chronic bronchial asthma may be considered a predisposing factor affecting individual susceptibility The spasmodic attacks, if frequent, lead to a reduction in the individual's vital capacity Aside from the pulmonary fibrosis, other pathological manifestations of silicosis such as bronchiectasis, emphysema, and right heart hypertrophy and dilatation, may be aggravated by this chronic condition

Chronic infections of a local or constitutional nature may be shown to influence materially the incidence of silicosis

As regards infection in general, Lanza (20) has stated that in all his experience he can recall seeing but one patient who died of pulmonary fibrosis uncomplicated The results of the survey in the Tri-State district emphasized the rôle played by infections in disabling silicosis, and mentioned the frequent occurrence of bronchial spirochetosis Recently, Proske has published reports of additional work along this same line which should do much to stimulate the taking of preventive measures to control such infections in the sinuses and dental regions as may serve as a source of these organisms

Infections developing along the respiratory tract are of importance Sinus infections may act by decreasing the efficiency of the upper respiratory tract in the removal of dust from the air passing to the lungs, and also they may be the source of infections that spread to the lower respiratory tract Acute pneumonic conditions as well as the more chronic lung changes, such as chronic bronchitis, bronchiectasis and bronchiolectasis, emphysema, and pleurisy, all tend to decrease the ability of the lung to rid itself of foreign materials, through lessened lymphatic

drainage and decreased power to force the bronchial secretions and foreign matter from the lungs. The dilated bronchi and areas of emphysema developing in persons as a result of abnormal demands made upon the lungs by glass blowers, divers, professional singers, trumpeters and the like seldom advance to the point where the individual offers any complaint until infection is present.

In a recent review and discussion of the subject of bronchiectasis, Christie emphasized the infective element as well as other pathological changes associated with the condition. The lung changes accompanying silicosis might be expected to lead to conditions favoring bacterial invasion. Some writers most familiar with the problem believe that the dense areas of fibrosis seen at autopsy or appearing as conglomerate shadows in the X-ray film possibly are dependent upon an infective process, either present before the absorption of silica or developing in an area of pulmonary fibrosis due to the action of silica.

TUBERCULOSIS AND SILICOSIS

In 1907 Summons of the Miners Phthisis Committee of Australia, reported that gold miners there who contracted silicosis died of tuberculosis.

The increased incidence of tuberculosis among occupational groups exposed to silica, has been clearly shown in every instance where this hazard exists. Britten summarized the report of the Registrar General of England and Wales for 1921 to 1923 inclusively and showed the occupational mortality rate for the group of trades classed as "Dusty Trades" to be from 3 to more than 10 times as high as the rate for all occupied and retired males (Table II)

Lanza and Vane (21) show by an analysis of the mortality experience of 12 life insurance companies for the period of 1915 to 1926, that the actual mortality from respiratory tuberculosis among the persons exposed to silica was about 3 times that of a group not exposed to silica When this comparison is limited to the rates for some of the occupations with a very great silica exposure such as metal mining sandstone and granite quarries, the excess is still more striking the rate being about 10 times that obtained in the non-silica-exposed group

The initial studies of silicosis by workers in South Africa were started by a demand upon the health authorities to determine the cause of the excessive mortality from tuberculosis, which was increasing at a rapid rate among the gold miners there. The study by Russell and associates of the health of granite workers was prompted in part by the excessive number of deaths reported as due to tuberculosis in the section of Vermont in which the granite industry is located.

Gardner's (11) statement that, "At least 75 per cent of those human beings who develop silicosis die of tuberculosis which may make its appearance at any stage of the disease," stresses the importance of the silicosis problem from the viewpoint of antituberculosis activities. Rist and Donbron advance the theory that there is no nodular fibrosis until the element of infection has entered the picture Such a theory however does not agree with experimental work which has shown that the nodules may be produced in the absence of evidence of infection.

Kettle (17) and Price and others have shown that the tubercle bacillus will grow more rapidly upon culture media to which a small amount of silica is introduced thus offering a favorable media for the growth of the organism. Gardner (8) has shown that animals exposed to silica when inoculated with a strain of tubercle bacilli of low virulence, will develop systemic tuberculosis and die while control animals not so exposed usually are not seriously affected by injections of such organisms.

PROGRESSIVE TENDENCY OF THE DISEASE

Since infection has been shown to play so important a rôle in the advanced stages of the disease the possible relationship of this infective element to the progressive tendency of the disease cannot be overlooked.

Irvine has stated that it is not so much what the condition of the silicotic is today as what it will become tomorrow Irvine emphasizes the tendency of the fibrosis to progress even though removed from exposure, and expresses his opinion that it is one of the most serious aspects of the whole silicosis problem. No remedy has been shown to be of value in elimination of the pulmonary fibrosis, although certain improvement in symptoms may be noted after the victim is removed from exposure. According to the observations made by Behme-Bochum, silicosis progressed after removal from exposure in 10 per cent of the cases the diagnosis was silicosis grade 1 in 40 per cent, grade 2 and in practically all other cases, grade 3 The course of silicosis among workers no longer exposed to silica dust is adequately stressed in the report of Russell, and the references discussed furnish evidence that, regardless of termination of exposure, silicotics may progress eventually to a more severe and even fatal condition. Such reports from workers most familiar with the condition surely serve to em-

phasize the seriousness of this occupational disease

Therefore, it may be stated that a full understanding of the true etiological factors accounting for the development of silicosis in a single instance requires detailed knowledge of the individual's occupational exposure past and present, together with facts obtained through a complete physical examination, with particular attention to positive evidence of old or recent respiratory infection Although a slight mention may be made of the predisposing cause, after all, in the great majority of cases, whether individuals will develop silicosis depends nearly entirely upon the concentration of free silica particles under 10 microns in diameter to which they may be exposed and the duration of such exposure

CLINICAL MANIFESTATIONS

Early in the development of uncomplicated silicosis, there is seldom any thing suggestive about the general appearance which would indicate that the individual is affected by a chronic lung disease Later, when shortness of breath is becoming evident, there may be a tendency for the worker to be less active and many gain weight Respiratory embarrassment gradually increases with the increasing pulmonary fibrosis, and hypertrophy of the accessory muscles of respiration is observed The anteroposterior diameter of the chest increases, there is a widening of the intercostal spaces, with lessening of the elasticity of the lungs, and the chest is best described as barrel-shaped or emphysematous type

The cardinal symptom is shortness of breath This, in early cases, may be observed only following exercise To elicit this symptom and estimate its degree, a uniform exercise test may be carried out as follows The individual places one foot upon a chair or firm stand, 18 inches in height, and raises his body to an erect position 25 times in 30 seconds Those with marked respiratory or cardiac disturbances cannot be subjected to such a test, but in the course of examining persons already employed or applying for work, few of such individuals will present themselves The pulse and respiration is taken with the examinee at rest immediately following the exercise test and after a 2 minute rest period It is evident that such a test is not one the results of which are affected by respiratory conditions only, but one which is influenced by various factors, such as weight, heart condition, age, general physical condition, and numerous metabolic differences It does serve as an indication of decreased capacity for work When we consider all factors, definite information

TABLE II —STANDARDIZED MORTALITY FROM RESPIRATORY TUBERCULOSIS IN OCCUPATIONS WITH RATES ABOVE AVERAGE, MALES AGE 20 TO 65 YEARS, 1921–1923, ENGLAND AND WALES

Occupation	Mortality rate (standardized)
All occupied and retired males	149 6
Tin and copper mines, underground workers not superintending staff	1886 0
Tin and copper mines, not superintending staff	1323 5
Grinders in the cutlery tools	1178 5
Metal grinders	636 7
Slate masons and slate workers	512 5
Potters' mill workers, slip makers, potters	411 4

concerning respiratory capacity is available Regardless of the presence of slight cardiac defects or changes due to age, etc , the individual with appreciable pulmonary fibrosis will exhibit not only shortness of breath following the exercise, but the characteristic altered respiratory rhythm The expiratory phase is markedly prolonged, often to such an extent that the rate of respiration is much less than in the case of a person with pulmonary infection or cardiac disturbance Due to loss of elasticity of the lung, the individual cannot empty his lungs rapidly enough to allow for a great increase in respiratory rate In fact, the rhythm approaches that of the asthmatic before exercise The condition may be differentiated from bronchial asthma by the absence of the rales and other clinical data In cases of well established silicosis, prolonged expiration may be elicited by careful observation during the course of physical examination, prior to any exercise test

The rôle played by cardiac deficiency may be determined by considering the records of the pulse (before, after, and following the rest period), and the blood pressure determinations

Closely associated with the development of shortness of breath manifested by the silicotic, is a variable cough When the cough first becomes noticeable, it is unproductive and is usually brought on by exertion Later it may be stimulated by the efforts required to carry on usual activity In most cases of uncomplicated silicosis, this cough is so slight that its presence will not be elicited without direct questioning or observation following exercise

Decreased chest expansion is also mentioned as characteristic of silicosis A marked decrease is seldom found until the condition has progressed to the stage at which there is evidence of a lessened capacity for work In the examination of nearly 3,000 hard coal miners, it was learned that the

average chest expansion of those with silicosis was about 75 per cent of the average for those in a control group. In the same study it was found that the average chest expansion of those in a group of totally disabled silicotics was about 50 per cent of the average for the controls.

In the industries studied, individuals with definite silicosis have been shown to suffer more frequently from temporary disabling respiratory infection than have the workers who present no signs of silicosis. The clinical manifestations of silicosis, complicated by pulmonary infection, tuberculous and non-tuberculous, cardiac defects extreme emphysema and pneumothorax, are as variable as are the signs and symptoms of the complicating conditions. The general appearance of an individual suffering from silicosis with infection or other disabling complications usually is indicative of the seriousness of the condition. Loss of strength and weight, prominent supraclavicular and infraclavicular spaces, muscular atrophy clubbing of the fingers, cyanosis, and edema are rather common findings.

The chest findings present a marked contrast to the usual negative findings elicited upon examination of the uncomplicated silicotic. Adventitious sounds are indicative of pulmonary infection or cardiac embarrassment. In the early complicated case, such alterations may be localized in but one section of the lung field, but later all portions of the lungs are found involved. The changes elicited upon palpation, percussion and auscultation, will depend upon the severity and type of the infection upon the extent of emphysema, pleural involvement, or pneumothorax present, and usually are interpreted readily

A non-tuberculous pulmonary infection complicating silicosis varies from that producing chronic bronchitis to extensive parenchymatous involvement leading to cavitation The sputum varies from simple slight, mucopurulent to thick, tenacious, blood streaked material with a foul gangrenous odor Mixed fusiform and spirochetal organisms, commonly found in the upper respiratory tract, have been shown to play a major rôle in the non-tuberculous pulmonary infections associated with silicosis (Proske and Smith)

Pulmonary tuberculosis has been shown to be a common terminal complication. It is usually present in a chronic fibroid form, and for this reason may exist for some time before laboratory examination of the sputum proves positive As in fibroid phthisis not complicating silicosis, animal inoculation with the sputum offers the most certain chance of establishing a definite diagnosis

Temperature varies with the extent and activity or acuteness of the infection complicating the silicosis, and the variation is seldom noticeable to the person affected until the very last few weeks or months of his life.

Several studies on urinary excretion of silica indicate that persons exposed to abnormal amounts will excrete correspondingly large amounts of silica. However excessive silica in the diet will produce a like increase in elimination, and must be considered. Furthermore, cessation of exposure does not cause an immediate marked decrease in silica excretion. Old silicotics, whose occupational exposure to silica dust had ceased 2 to 10 years previously were found to be eliminating more than twice the amount of that eliminated by a non-exposed group on the same diet (35) Thus, excessive silica excretion indicates merely excessive silica intake at some time, and its relation to present exposure must be considered with several qualifications.

Tables III and IV indicate the frequency with which the subjective and clinical manifestations occurred in a group of 616 anthracite coal miners, found to have anthracosilicosis, and 135 totally disabled former hard coal miners.

ROENTGENOLOGICAL FINDINGS

While the roentgenological findings of simple silicosis are characteristic, it is not possible to diagnose silicosis definitely upon X-ray findings alone, they should be considered with the medical and clinical manifestations.

FLUOROSCOPIC EXAMINATION

Although a fluoroscopic examination is not relied upon to detect details of pulmonary changes common in silicosis, it does offer certain advantages Decrease in motility of the diaphragm may be measured This decrease varies from slight to practical fixation and parallels the respiratory embarrassment shown upon exercise Frequently adhesions between the visceral and diaphragmatic pleura may be demonstrated. Knowledge obtained by oblique and lateral fluoroscopic examination of the chest is helpful when for any reason stereoscopic films are not secured The practice of examining an individual by means of the fluoroscope prior to taking an X-ray of the chest, in advanced cases at least furnishes information which is valuable in determining the X-ray penetration needed for a good film

The characteristic X ray film of the chest will show in the case of simple silicosis, symmetrically distributed, clearly defined nodular shadows, from 1 to 6 millimeters in diameter As the condition advances, the nodular shadows increase in size

TABLE III —FREQUENCY OF COMPLAINTS COMMONLY VOLUNTEERED BY WORKERS HAVING ANTHRACOSILICOSIS SIMPLE AND WITH COMPLICATIONS, COMPARED WITH A GROUP TOTALLY DISABLED BY ANTHRACOSILICOSIS

Group	Number	Percentage complaining of		
		Shortness of breath	Cough	Weakness
Unaffected workers (controls)	361	6 4	2 2	0 8
Those with simple anthracosilicosis	219	32 7	10 7	2 33
Those with anthracosilicosis and infection	397	48 1	22 9	7 9
Those totally disabled by anthracosilicosis	135	100 0	88 0	100 0

and eventually are found to appear coalesced, this change is gradual and the coalesced areas gradually form large, dense, well defined shadows With this increase in fibrosis, a compensatory emphysematous condition gradually develops, as demonstrated in the film by scattered areas of increased transparency When the silicotic nodules develop subpleurally, the visceral and parietal pleura may become involved with the formation of adhesions Some authorities are of the opinion that usually these large conglomerate areas of fibrosis which produce the massive shadows on the X-ray film, and the pleural adhesions are the result of either previous infection and resulting scar tissue at that site or concomitant infection as the nodules develop

It is not possible to interpret changes preceding the nodular shadows characteristic of silicosis as presilicotic, unless serial films at different periods of exposure are available The increase in linear marking, enlarged hilus, and grainy diffuse shadows are all within the limits of what may be considered an essentially negative film The increase in pulmonary fibrosis producing the slightly irregular if not abnormal markings may be the result of chronic respiratory infection, circulatory changes, age, etc

The character of the film shadows, once infection has played a part, is dependent upon the severity and type of infection and upon whether infection preceded or followed the exposure to silica The shadows are less symmetrically distributed, their borders are less defined, the nodular shadows are of such a character that the term "mottling" has been suggested as more descriptive Pleural thickening and adhesions frequently are demonstrated and the mediastinum, especially after cavities have developed, often is displaced

TABLE IV —PERCENTAGE OF WORKERS HAVING SIMPLE ANTHRACOSILICOSIS AND ANTHRACOSILICOSIS WITH INFECTION, SHOWING CERTAIN PHYSICAL FINDINGS (AFTER EXERCISE TEST)

Group	Number	Percentage showing			
		Shortness of breath	Altered breath sounds and/or impaired resonance	Persistent râles	Prolonged expiration
Unaffected workers (controls)	361	1 6	26 5	3 3	0 6
Those with simple anthracosilicosis	219	41 6	84 6	20 6	40 2
Those with anthracosilicosis and infection	397	58 7	93 7	50 4	49 9
Totally disabled by anthracosilicosis	135	100 0	95 0	51 8	78 0*

*Without exercise.

The diaphragm frequently is irregular in outline, and localized emphysema may be demonstrated by the areas of decreased roentgenographic density Localized areas of a massive pneumothorax are sometimes found

DIAGNOSIS

Diagnosis of silicosis is based upon occupational and clinical history, and physical, laboratory, and X-ray findings Although a diagnosis of silicosis should not be made upon X-ray findings alone, neither should a positive diagnosis be made without a good chest film Postmortem diagnosis may be made by examination of the lung, pathologically and chemically

The physician, experienced in the diagnosis of silicosis, familiar with the character of work usually performed by an individual found suffering from the disease, may fairly well demonstrate decreased capacity for work which may be attributed to simple silicosis To determine the degree of disability, or the cause of disability after infection has entered the picture, usually requires clinical observation for some time, affording an opportunity for more detailed and repeated examination of the individual

OCCUPATIONAL HISTORY

Since knowledge regarding previous occupational exposure is so important in the final interpretation of clinical and X-ray findings and in the proper placing of individuals at work where they may safely carry on, detailed information of this nature should be secured The record should

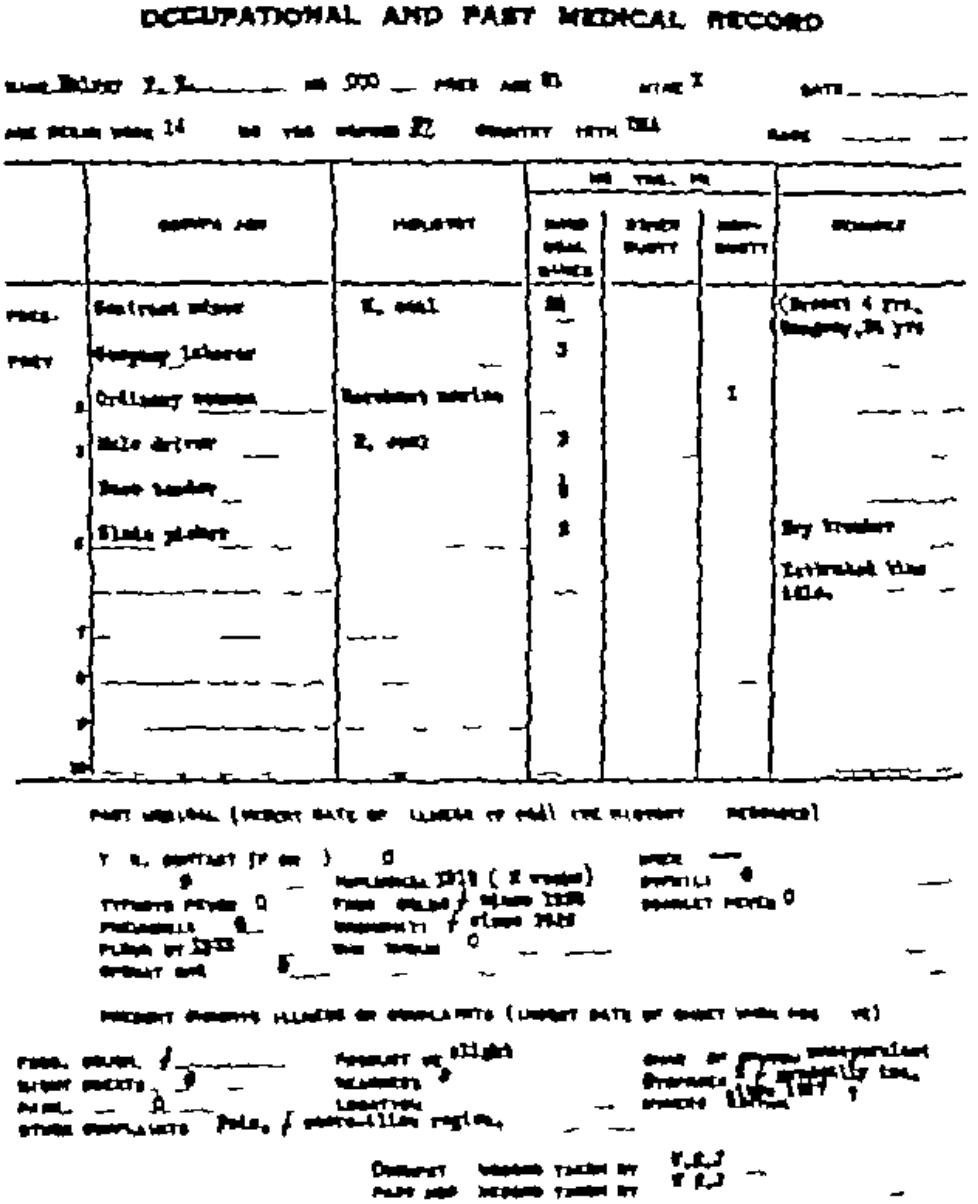

Fig. 2. Record chart showing occupational and past medical record

indicate each specific occupation in each industry in which the individual has been employed and the duration of employment at each job. If the record begins with the present occupation and lists each preceding one back to the time the individual started to work the data will probably be more complete. Figure 2 shows a form which was found practical in recording occupational history upon a group of hard coal miners.

PREVENTION OF SILICOSIS

This phase of the silicosis problem may be considered advantageously under two main divisions, medical and mechanical.

Medical. Pre-employment and periodic physical and roentgenological examination should be made of all employees engaged in industrial processes where there is a potential, if not actual, exposure to excessive concentrations of silica in the atmosphere. The medical personnel making these examinations should be familiar with the industrial processes in which the individual is to be employed.

In fairness to the individual, his fellow workers, industry and even the public at large, an individual with evidence of active tuberculosis or extensive healed lesions should not be employed in an atmosphere where there may be exposure to silica dust. The infected individual's condition may be aggravated by such exposure. His fellow workers may become exposed under conditions which, were it not for the presence of silica, might

not be dangerous Eventually industry will bear the burden of compensation for injury to the health of the employee and possibly some of his co-workers, for with existing conditions, the prevention and control of tuberculosis among the general population will be more difficult In the absence of infection, silicosis is a slowly progressing disease and develops at such a rate that the individual affected may not become disabled during his ordinary working life Therefore, if infection can be lessened, the silicosis problem may be controlled much more readily

Periodic physical examination will serve to detect early evidence of infection and abnormal pulmonary changes resulting from dust exposure It will then be possible to correct the conditions causing the pulmonary fibrosis, and to prevent the development of disabling pulmonary disease Unless active pulmonary infection is diagnosed, the individual with a beginning fibrosis or non-disabling silicosis may be safely continued at his present employment, provided the dusty conditions causing it are eliminated Usually the physician familiar with the patient's condition and the occupational environment to which he is exposed is in the best position to advise his retention or removal from the industry

Engineering or mechanical control Prevention of silicosis from the viewpoint of engineering and mechanical control lies in the efficiency of such methods as may be adopted (1) to prevent the escape of siliceous dust into the workroom atmosphere, (2) to remove efficiently dust from the atmosphere in processes in which its escape is not preventable, and (3) to provide mechanical personal protective equipment—for emergency use, or in the operation of such processes as are used only temporarily, or for but short intervals of the working day

Certain processes readily permit the trapping of the dust at its source, in other processes apparatus may be completely enclosed, thus preventing the escape of dust at any point during operation Examples of such are the jack hammer with dust trap attached and the enclosed abrasive processes in which mechanically the product being ground is passed in and out without escape of abrasive material used

The dust in the air of some quarters may be removed by an air filtering arrangement which will secure a rapid exchange of clean air for dusty air Water sprays and other wetting down methods serve to keep general atmospheres clean or to remove the offending silica Whenever practical, dusty processes should be isolated from other divisions of the industry, for in this way, the number of employees subjected to a potential hazard is reduced to a minimum

Occasionally, without decrease in efficiency or increase in cost, satisfactory substitute materials which contain less silica may be found

Sometimes the cleaning of work places may constitute a source of atmospheric pollution with silica dust. Vacuum cleaning and wet methods may solve this problem satisfactorily, when such methods are not feasible, the cleaning should be done outside working hours when there will be the least number of persons exposed For the time involved, those doing the cleaning may be protected by respirators or positive pressure helmets

In the driving of tunnels and in mining which may necessitate the removal of siliceous rock, blasting operations account for a large amount of atmospheric pollution It has been found practical in many instances to do this blasting after regular working hours or between shifts, sufficient time being allowed to elapse for the air to clear Water sprays released simultaneously with blasting have been carried out to prevent general dispersion of the dust to other workings in the vicinity of blasting operations

The part played by a study of workroom environment by qualified personnel is essential to successful control of a silicosis hazard Analysis of workroom air prior to the installation of methods for keeping the atmosphere safe, serves to indicate the necessity for the institution of methods for dust control and serves to determine the effectiveness of measures employed thereafter Periodic inspection of all equipment designed for the prevention of atmospheric contamination should be carried out at intervals found to be satisfactory

Close co-operation between the engineering and medical personnel is essential for economical and safe control of the dust hazard No one method or equipment has proved effective and practical, but the adoption of those most practical and safe under capable direction may be relied upon to prevent conditions which will cause silicosis

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HEAT AND MUSCULAR WORK[1]

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MY first experience with the effects of heat on the working man was in September, 1914 It was at this time that I entered the field of industrial medicine About 5 00 o'clock one afternoon of a very hot and sultry day, the men from the open hearth carried into our small clinic a man with intense cramps in his arms, legs, and abdomen They gave the story that the man had been working around the hot furnace all day and had been drinking too much cold water I did not realize what the future had in store and that I was to see many more of these cases in my work as a physician in industry

HISTORICAL

Heat stroke or sun stroke is the oldest known disease The ancients associated the disease with Sirius, the dog star, and dog days, probably because in the summer months Sirius follows the sun and is visible in the evening twilight The oldest records of the disease are the biblical cases In the 4th Book of Kings, Chapter IV, is found "And the child grew and on a certain day when he went out to his father to the reapers, he said to his father My head acheth, my head acheth and when he had taken him and brought him to his mother she set him on her knees until noon and then he died" In the Book of Jude, Chapter VIII, is found, "And her husband was Manasses who died at the time of the barley harvest where he was standing over them that bound sheaves in the field and the heat came upon his head and he died in Bethulia his own City and was buried there with his fathers"

Wakefield and Hall call attention to the confusion of heat with apoplexy as illustrated by Forestus in 1562, and Baglivi, of Rome, in 1694 and 1695 called attention to an epidemic of apoplexy which was confused with sun stroke Lancisi, according to Levick, was the first to publish evidence of the influence of hygrometry in the etiology of heat effects In 1789 Dr Benjamin Rush called attention to a disorder occasioned by drinking cold water in warm weather and described the symptoms of heat stroke very accurately Andral, of Paris, was the first to note the relation between high atmospheric temperatures and heat conditions Condie, in 1858, described heat stroke occurring in places other than in the sunlight He was the first to emphasize the humidity of the air as an important etiological factor In 1858, Claude Bernard considered the cause of death in heat conditions to be due to purely physical causes, that is, elevation of the blood to such a high temperature In 1872, H C Wood noted "The more violently a muscle is made to contract before subjection to heat, the sooner it becomes paralyzed" Dr R R Sayers and Sarah Davenport of the United States Public Health Service published (April 8, 1927) reports with complete bibliography, giving historical data of heat

THE PRODUCTION AND LOSS OF HEAT

Under normal conditions the human body produces more heat than is necessary to maintain the body temperature This excess heat is given off from the body in three ways (1) by conduction and convection, (2) by radiation, and (3) by evaporation Heat can be lost by conduction and convection only when the surrounding air temperature is lower than the body temperature and by radiation only when the surrounding objects are at a lower temperature When the surrounding objects are at a temperature higher than that of the body, the body absorbs heat from them, such for instance as from furnaces, red hot metals, or the sun When the body cannot lose sufficient heat by these two methods the sweat glands come into action and produce sweat which by evaporating causes heat to be lost from the surface of the body The amount of heat which can be lost by evaporation depends on the temperature and the amount of moisture already in the atmosphere, the higher the humidity, the less evaporation Air currents or wind also play an important rôle in heat loss, due to the fact that they cause the air in contact with the body to be changed and hence hasten heat loss However, when the air temperature is well above body temperature, air movement may have the reverse effect, i e, hinder heat loss, especially if the humidity is high If the body is unable to lose sufficient heat, the body temperature will of course rise

The amount of heat which the body produces increases markedly when a person performs any

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sort of muscular work. Every time a muscle contracts, an extra amount of heat is produced in the muscle. When the person is performing heavy muscular labor this great amount of excess heat must be lost immediately if the body temperature is to be maintained. In physical work in high temperature and humidity therefore, there is a marked increase in heat production due to the work combined with a poorer chance for the body to lose heat to the surrounding atmosphere.

What then are the results of working under these unfavorable atmospheric conditions? In the first place, *high temperature especially if associated* with a high humidity, limits a man's capacity for muscular work. Second, if the atmospheric conditions are extreme clinical symptoms of heat cramp heat exhaustion, and heat stroke may result.

Considering first the early onset of fatigue when working in hot atmospheres, ample experimental and practical evidence is available to prove that a man cannot perform as much physical work when the external temperature is high It is not just discomfort or laziness on the part of the worker when he fails to turn out as much work on a hot day McConnell and Yaglou, for example have shown that at a relative humidity of 60 per cent a person can perform about twice as much work in a temperature of 90 degrees F as at 110 degrees F and five times more work than at 120 degrees F What then happens in the muscles or in the body as a whole which leads to this early exhaustion?

CHEMICAL CHANGES

The chemical changes which take place in a muscle during contraction and which lead to fatigue and exhaustion of the muscle, have been the subject of much research. According to the present theory the energy for the muscle contraction is derived from the breakdown of phosphocreatine into creatine and phosphoric *acid which occurs during* muscular contraction This must be resynthesized continually if muscular contractions are to continue The energy *for this resynthesis is presumably derived* indirectly from the breakdown of sugar into lactic *acid which also occurs when a muscle* contracts. It has been shown that a portion of the lactic acid $^1/_4$ to $^1/_6$ is oxidized and that the energy thus liberated is utilized to resynthesize the remainder of the lactic acid back into glycogen If the lactic acid *accumulates to sufficient* concentration, it becomes a limiting factor to the amount of work which a muscle can perform. In physical exercise so strenuous that one is completely exhausted in a short time, the lactic acid may accumulate so rapidly that its oxidation cannot begin to keep pace with its formation, and under these conditions the lactic acid in the muscles and blood may accumulate in sufficiently large amounts to lead to complete exhaustion. In prolonged moderate work, however even at high temperature the body becomes exhausted without any marked accumulation of lactic acid in the body as a whole and without exhaustion of the supply of sugar (Dill and Edwards, etc.) On the other hand, McCurdy (1932) states My belief at present is that we are dealing with a toxic *spasm of the* voluntary muscles caused by the accumulation of lactic acid and probably intensified by some disorder of metabolism and an added stage of fatigue carried further than usual because of the influence of high temperature and *high humidity* upon very active muscle contractions." It is, therefore, impossible at present to explain the muscular exhaustion experienced in unfavorable atmospheric conditions on the basis of the chemical changes taking place within the skeletal muscle It has, therefore been suggested that the cause of the exhaustion probably is referable to the heart. The heart rate increases not only with muscular exercise and with a rise in body temperature but also with external temperature even though the body temperature may change but little Dill, Edwards, and others have suggested that fatigue of the heart muscle, possibly due to the accumulation of lactic acid in it, may be responsible for physical exhaustion when man works at high temperature, since exhaustion comes when the heart has attained its maximum rate

CLINICAL MANIFESTATIONS

Turning now to the clinical side of the problem, the three well known clinical conditions which result from heavy physical work in a high temperature (and humidity) when the body is unable to compensate for these conditions, are (1) heat cramp (2) heat exhaustion, (3) heat stroke.

HEAT CRAMPS

Here is a picture of the symptoms of heat cramps Usually in July or August, a hot, sultry day the man working in say the drop forge, gets up early for his turn, eats no breakfast, or at most takes a cup of coffee and hurries to the plant. He works about an hour feels thirsty and drinks freely of water About a half hour later he has a spell at work, and eats a cold sandwich probably of thick bread with some kind of meat and onions, returns to his work, drinks more water and soon notices that he feels a little queer is sweating

profusely, has a headache, and is compelled to quit and steps out into the air Immediately he feels a twitching and pain in the muscles of his legs and arms and is forced to call for help His co-workers put him on a stretcher and he is rushed to the clinic. When he arrives, you see a man who is pale, cold and clammy, down and out The degree of muscle cramps with associated pain, etc , depends upon the severity of the attack One of two conditions exists, there is either a state of exhaustion where the man practically passes out, or a state where he has such violent cramps in his arms, legs or abdomen that he cries out with pain On recovery, you learn that he did not get much sleep the night before, that he has not been eating regularly, that he has been drinking a little more than usual, that he is constipated having paid no attention to his bowel movements, and in general, that he has not given much thought to his health and personal hygiene

Symptoms of heat cramp Examination reveals characteristic symptoms and signs

1 *General* The cramps are always preceded by marked sweating The cramps are painful, tonic spasms of any skeletal muscle but usually of those most actively in use, chiefly the muscles of the calf, the flexors of forearm, and of abdominal wall The spasms occur at the slightest movement The temperature varies from 95 degrees to 102 degrees F The pulse is slightly rapid (usually not over 90 a minute), and thready Respiration is rapid The skin is cool and clammy and the blood pressure is low Talbott reported variation from 118/68 to 132/84 Other symptoms may include nausea, vomiting, diarrhea, dizziness, and mental depression

2 *Blood change* (1) The blood chlorides are very low, the reduction being between 5 and 14 per cent in blood salts (2) These changes are no greater than in moderate exercise, namely, (a) (HCO_3) slightly below average, (b) lactate and inorganic phosphate of serum increased slightly, (c) protein ions increased because of dehydration with concentration of blood (3) The total base (serum) is low (4) The red blood cells are concentrated (5) The cell hemoglobin concentration is slightly decreased (6) The total white blood cells are slightly increased

3 *Urine* The chlorides are very low or absent, nitrogen is increased, possibly due to utilization of tissue for food, there is low urine excretion due to water loss in sweat. There does not seem to be any lack of functioning of kidneys as a direct result of heat, there is merely an indirect result due to loss of water and salt through sweat

Etiology The present viewpoint is that the loss of base, chlorides, and water from the body in the sweat is the primary factor in the cause of heat cramp (Talbott) The basis for this lies in three facts (1) the great amount of chlorides lost in the sweat, (2) the low chlorides in the blood and urine reported in cramp cases, and (3) the effectiveness of treating such cases with intravenous sodium chloride

Normally we take in from 10 to 15 grams of sodium chloride per day in the food In the kidney, water, salt, etc , passes out in the glomerular capsule, and water (with other substances) is reabsorbed in the tubules Sodium chloride may or may not be reabsorbed depending on the concentration of sodium chloride in blood plasma This maintains the sodium chloride in the blood at a constant level under normal conditions The normal sodium chloride loss in the urine is about 15 grams per day When this falls below 3 grams of sodium chloride per day, a dangerous level has been reached, according to Talbott and his co-workers When the sweat glands are called into action, there is a marked loss of salt and water from the skin Here there is no regulatory function as in the kidney to maintain the blood chlorides at their normal level The amount of salt lost in the sweat varies with the individual, the external air temperature and humidity, the duration of exposure and the degree of acclimatization The chloride content increases with duration of sweating Variations of sodium chloride in the sweat of 06 to 6 per cent have been reported The salt content, however, decreases with acclimatization after about 3 to 5 days (Dill, Talbott, etc) The ratio of sodium potassium in sweat varies in different individuals from 5 1 to 3 2, according to the different reports in the literature The total volume of sweat produced in a day when working at high temperatures may be as much as 5 to 6 liters per 24 hours with a total sodium chloride loss of 20 to 25 grams per day Just how salt loss through the sweat can lead to muscle cramps is not known This is not surprising since we, even now, know very little about muscle contraction

Sodium is the predominant base in the blood serum and extracellular fluids, being about 18 times as abundant as potassium, whereas potassium is the predominant base in human muscle and blood cells (intracellular) Since it is sodium which is chiefly lost in the sweat, one can assume that the sodium chloride passes from the blood to the sweat glands and that the salt of extracellular fluid, in order to maintain salt equilibrium, tends to pass into the blood (There is, however, no direct proof of chloride depletion of extracellular fluid) Whether the loss of extracellular sodium

chloride in turn leads to the passage of potassium from the cells into the extracellular fluid under these conditions is not known. If there were a loss of potassium from the muscle cells, one would expect that treatment with a solution of sodium chloride and potassium combined would be better than sodium alone but this has not proved to be the case. It is at present impossible to explain how a loss of salt in the sweat leads to muscular cramps

With regard to the possible rôle which sugar plays in the etiology and treatment of heat cramp, the general view at present is that it is not an essential factor (Baetjer) That profuse sweating alone does not lead to hypoglycemia, was shown by Marchionini and Ottenstein who found after 30 minutes of profuse sweating, a rise in blood sugar from 100 to 145 milligrams per cent. However with exercise and a longer duration of sweating, this may not be the case. Furthermore, treatment of heat cramp with glucose solutions has been reported by some to be unsuccessful. Talbott and Michelsen reported blood sugars of 95 to 114 milligrams per 100 cubic centimeters blood in their 7 cases of heat cramp at Boulder Dam, indicating therefore no significant change, and 95 milligrams as the average for a group of normal workmen at the same time Despite this, our experience with sugar is most gratifying, not alone, but in conjunction with salt. There is always shock present in heat exhaustion and heat cramps, and the value of glucose solutions is well founded by Crile and his co-workers Laird also has shown the value of sugar in the fatigue accompanying heat exhaustion

Podolsky further has shown that sugar is a stimulant, needed under such conditions

Dextrose supplies a source of food and energy that is immediately available. It tends to combat acidosis, protects the liver by contributing to glycogen storage satisfies thirst, and increases volume of circulating fluids that might be deficient as a result of vomiting and diarrhea Crile in a personal communication says "It has been established that glucose carries energy to replace that which is being lost and salt solution is the electrolytic basis of protoplasm" McCurdy believes that "since glycogen has been diminished greatly with an excessive production of lactic acid, because of acidosis, it can be reconverted into glycogen by the intravenous injection of 1 per cent glucose 300 to 500 cubic centimeters with saline to replace the chlorides of the blood and diminish dehydration (This is questioned) And so it would seem that since temperature affects the heart rate, and complete fatigue of the heart muscle causes exhaustion then sugar does have a place in the prevention and treatment.

Treatment The treatment of heat cramps will depend somewhat on the severity of the cramps Mild cases will recover if put to bed and covered with blankets and external heat is applied We usually give these mild cases, by mouth, a mixture of 10 grains of salt and 5 grains of dextrose and repeat as needed In the cases of low temperature, if the patient is not sweating, we believe that it is necessary to keep him well covered and to supply external heat until his temperature reaches normal and he is sweating freely We have noted that if allowed to expose his arms or legs, immediately they will become cramped. In the severe cases, it is our practice to give intravenously 5 per cent glucose in normal saline administered 500 cubic centimeters to 1 liter or more Other workers in heat conditions recommend the administration of intravenous saline without the glucose Mixtures of sodium and potassium or of the usual blood salts have been tried but seem to be of no advantage In fact if potassium is added in too great quantity a diuretic effect may be obtained

Prevention. As I stated before our first experience with heat cramps was in 1914 and from then to 1932 we were constantly looking for a way in which to prevent heat exhaustion and heat cramps in those departments of the industry where heat is a hazard. In making a survey of the plants and in watching the habits of the men in these various departments, we made the following observations We noted that, in the crucible where the men were permitted between turns to leave the job, they crossed the street to get a glass of beer We noted that they always put salt in the beer and that they always returned to the job with pretzels. We also observed that although this was one of the hottest places, the incidents of heat exhaustion were less than in others. In another department, the men insisted on having at their disposal Jamaica ginger In yet another department the men insisted on having a barrel of water and into this they poured a package of rolled oats This was cleaned daily We noted that the incidents of heat exhaustion were not marked from this department In one plant, the men were accustomed to eating gum drops and in another plant, they insisted on having peppermint lozenges In still another when we asked about the heat conditions, the superintendent advised me that there was no need to go to a certain furnace because all the men employed were negroes We visited this furnace and on observation we noted that one negro would take something from his pocket every now and then and

chew it When we asked him what he was chewing, he said, "peanuts" and on asking why he ate peanuts, he said, "I don't know, boss, but the boys before me just told me that if I ate peanuts, I no get them heat cramps" What he was eating was salted peanuts and we learned that this custom had been handed down for a number of years, which was the reason for no heat cramps from that particular furnace You will note from these observations that the men themselves had learned certain things to prevent these conditions The beer with the salt, the gum drops, the peppermint candy, the oatmeal water from which they secured potassium salts, and the salted peanuts, all led us to believe that there was some preventive measure in salt and sugar

Moss credits Haldane with the suggestion that the cramps suffered by miners are due to salt losses Moss' investigations among miners led him to conclude that during work in high temperatures, some of the men suffered from a great shortage of chlorides in the blood, caused by a combination of excessive sweating and drinking of water with attacks of cramps resulting He did not believe that the sweating alone could be responsible for the shortage, since the tendency would be toward a concentration of chlorides in the blood The excessive drinking of water by the miners, due probably to the dryness of the mouth and throat, tended to dilute the blood until, in some of the men examined, the excretion of chlorides by the kidneys showed a marked decrease from normal, despite the enormous excess of urine passed In order to relieve cramps and also fatigue, Moss recommended the addition of salt to the water drunk by the miners

On the basis of this discussion, it would appear that the most efficient method of preventing heat cramp would be to replace the salt lost in the sweat by taking extra salt by mouth This has been recommended for some years and has been in practice in a number of industries Although no statistical studies or controlled experimental studies have been published to prove the efficiency of this, those interested in the results seem to have been convinced that the incidents of cramp have been lessened since the introduction of this preventive measure We believe these figures to be the first reported During the years 1926, 1927, and 1928, of an average yearly employment of 8800, we had 380 heat cases with 2 deaths During the years 1929, 1930, 1931, and 1932, we tried various preventive measures based on our observations from 1914 to 1929 After these observations and a review of the work done by others, we decided to use tablets of dextrose and salt These we placed in all departments with a heat hazard and encouraged the men to take a tablet with each drink of water From 1933 to 1935 we had 196 heat cases, no deaths, with an employment of a yearly average of 7800, and we noted that what cases we did have, were of a much milder degree, in fact, we have not had a severe case of heat cramps during the past 3 years Whereas we formerly asked the men not to drink too much water, with the use of the tablets we found that they could drink practically all that they wanted without any harm In another plant during the year of 1931 from 8500 men we had 680 heat cases, but after installing the dispensers and tablets in the year 1935 in the same plant with 9500 men, we had 305 heat cases with a notation that there was a marked lessening degree in the severity of all of them The tablet used consisted of 5 grains of dextrose and 5 grains of salt The salt may be added either to the drinking water or furnished in tablet form to be taken with each drink of water The concentration of sodium chloride which has been recommended for drinking water varies greatly Concentrations of 0 1 per cent sodium chloride for acclimatized workers up to 1 per cent sodium chloride solutions have been suggested It is obvious that no arbitrary amount can be set since the salt loss itself depends on so many conditions Those who recommend salt alone advise a compressed tablet of 16 grains, and suggest that one tablet be taken with each glass of water, assuming that the workers take about 2 or 3 glasses of water each hour during the working period It has been suggested that potassium might be added with benefit but there is no evidence that this is an improvement over the sodium chloride alone If this is done, it should be added in small amounts, as the ingestion of potassium may provoke diuresis, and under some circumstances is reported to accelerate the excretion of sodium from the kidneys

Whether there is any danger from excessive sodium chloride intake as a preventive measure is not known In healthy men who are losing large amounts of sodium chloride in their sweat each day, the only danger from taking extra salt would be from a local dehydrating effect on the stomach mucosa where the compressed salt tablets lodge while dissolving, whether this is a potential danger is not known Furthermore, the use of enteric coated tablets would avoid this In cases of preexisting nephritis or edema, of course, sodium chloride tablets should not be taken, but it is quite unlikely that these patients would be holding heavy jobs in high temperature and humidity Whether excess sodium chloride intake is a factor

leading to hypertension, one cannot say as the evidence is contradictory and unconvincing. Baird and Haldane reported that 30 to 40 grams sodium chloride in one day with 500 cubic centimeters to 3 liters of water caused visible edema. It is possible that the men who are not losing much sweat but are taking the extra salt might be getting an excess of sodium chloride. It is, however scarcely likely that a workman who is not sweating, would take more than 10 tablets containing 16 grains of sodium chloride each, which even with a normal salt intake in the diet, would scarcely amount to as much as 30 grams of sodium chloride per day. Also there is the question of adding carbon dioxide, salt and sugar to the drinking water.

Predisposing factors. Alcoholic bouts are a predisposing factor to heat cramps because of the attending decrease in food consumption with its salt. If accompanied by a gastric irritation with vomiting, an extra amount of salt would be lost from the body. Furthermore, the consumption of alcohol leads to peripheral vasodilatation and an increase in pulse rate, thus placing an added burden on the circulatory system.

Vomiting and diarrhea are also a predisposing factor because of the loss of chlorides from the digestive tract.

Poor living conditions seem to play some part in predisposing to heat cramp and exhaustion, etc. Bock and Dill state that in the summer of 1931 at Boulder City (Hoover dam) a number of deaths occurred among the workmen with a high incidence of heat prostration, while in 1932 only a few cases of cramps occurred. Although the temperature was higher in 1931 the significant difference appeared to be due to better housing conditions which included air-conditioned dormitories, and better food during 1932.

The salt content of the diet would also be important, since a high salt intake would naturally tend to replace its loss in the sweat, and vice versa.

It is an interesting fact that in the steel industry frequently the most severe cases of heat collapse occur on occasional warm days in the cooler months, for example in October. This is quite readily understood since the body becomes acclimatized to the external temperature whether it is warm or cool and exposure to a sudden change in temperature finds both the vasomotor mechanism and sweat glands ill prepared to meet this change in temperature.

HEAT EXHAUSTION

Symptoms. The patient is pale, cold, clammy, down and out with weakness, exhaustion and dizziness. The blood pressure is low; the pulse is rapid—average 80; the skin is cool and damp; the temperature is normal, or slightly below or above. Recent reports of experiments at Youngstown indicate that the chemical analysis of blood and urine showed no deviation from normal. Nausea and diarrhea were noted 5 times in 350 cases.

Etiology. The cause of heat exhaustion is not clearly understood, nor is it known why under the same conditions of physical work and environmental temperature, one man will develop cramps and the other will show exhaustion or prostration. Both conditions have somewhat the same general symptoms and both are brought on by physical work in high temperature with marked sweating. One might assume, therefore, a common etiological background. It would appear from recent work, however, that this may not be true, since at least in some cases of exhaustion, no fall in the sodium chloride content of the blood was observed, whereas this appears to be typical in cases of heat cramp. Then we have some men who are critically heat exhausted and later develop cramps. We have experienced cases in which a man was placed at rest in bed in the Emergency Hospital and apparently had recovered from heat exhaustion. He was allowed to go home but some hours later we were called and found him in a severe condition of muscle cramps.

It seems unlikely that the accumulation of lactic acid or the depletion of fuel supply (sugar) in the body as a whole play any important part in heat exhaustion. Talbott and Michelsen found no marked increase in the blood lactic acid in their heat cases and no hypoglycemia and, as explained, in complete fatigue from muscular work in high temperatures, there is no marked increase in the blood lactic acid. It appears likely that the condition of heat exhaustion is due ultimately to a collapse of the circulatory system. The heart rate is rapid; the blood pressure is low; especially the venous pressure as evidenced by the collapsed condition of the veins in some cases, and the blood is concentrated to such a degree that in extreme cases, the blood samples obtained from the vein frequently appear thick and syrupy. The cause of the collapse of the circulation is not known, whether it be fatigue of the heart muscle, stagnation of blood in the capillaries, or loss of salt and water in the sweat with a resulting decrease in blood volume, or a combination of these or some other factor, cannot be said. The condition resembles somewhat the clinical aspects of shock, although here we have no evidence that any toxic substance has been formed, nor any evidence of extravasation. One is impressed with

the similarity between heat exhaustion and the condition exhibited by dogs following suprarenalectomy In these cases Harrop has shown that a marked loss of sodium chloride occurs through the kidneys The animals show extreme muscular exhaustion, the blood is concentrated, and the sodium chloride in the serum is decreased

Treatment The same as in heat cramps is applied For mild cases bed, heat, salt and sugar For severe cases heat, intravenous injection of salt and dextrose

There is always to be considered the question of water metabolism which is closely associated with heat regulation and in turn with circulation and respiration We do know that water metabolism is influenced by food and work Then there comes the question of the utilization of water by the tissues Also there is the question of a thermal control center

HEAT STROKE

The symptoms of heat stroke are manifested in a very high temperature, as high as to 110 degrees F The pulse is very rapid, the blood pressure is high, the skin is usually hot and flushed although it may be moist, respiration is deep and labored The muscles are relaxed or twitching There is loss of consciousness with convulsions Autopsy shows congestion and hemorrhage of the brain and meninges

The onset may be gradual with mental excitement or depression and a dryness of mouth and skin, or it may be sudden with delirium, stupor or coma The skin is hot, and reflexes are absent

Treatment Therapeutic measures include water spray and fans with rubbing of skin, ice baths, etc , and prolonged rest in bed

OBSERVATION

Although the etiology may be the same, and the course run by a patient with heat exhaustion may follow a definite sequence, each case is a problem in itself

In heat exhaustion with cramps, the temperature is subnormal in practically every case When cramps are present, the temperature may be subnormal, normal, or there may be a rise in temperature as high as 101 to 102 degrees F At the onset of a case of heat exhaustion, there is a period in which all sweating ceases If exertion is continued, weakness comes on

Cramps usually appear after excessive sweating begins In the worst cases, sweating goes on for a prolonged period, in fatalities it continues until complete collapse

Most cases do poorly with morphia although it may be necessary to use it for pain Cardiac pain may be severe with violent contractions that cause heaving of the precordial area

There may be patients who have felt bad, and who, with stoppage of sweating or profuse sweating, collapse as soon as they are exposed to a cooler temperature, as going outside of a building to the open air

When a patient in collapse and with dry skin begins to sweat, improvement begins Temperature must be watched carefully so as not to apply heat after return to normal temperature

Dehydration can take place to the point that vessel walls collapse, the volume of blood decreases, becoming thick and syrupy in character and black in color

It has been necessary to bandage extremities One gains the impression that there is not enough volume to the blood to maintain circulation There is a point when there seems to be a complete vasomotor collapse Many men may work an entire shift without evidence of cramps, but develop them after leaving the job or upon arriving at home

Many cases seem very mild when first brought into the dispensary but grow worse while in bed during the next hour or two One should guard against permitting patients to get out of bed and to walk if they have cramps

ETIOLOGY OF HEAT STROKE

The underlying mechanism in heat stroke is probably quite different from that involved in heat cramp There are a number of theories for the cause of heat stroke One is that autointoxication results from the action of heat on the body tissues Another is that the heat regulating center in the brain breaks down Another is that the essential cause of heat stroke is acidosis This theory is largely based on experimentally produced hyperpyrexia in animals which have no sweat glands Hall and Wakefield, and Marsh showed on dogs and rabbits, respectively, that there was a marked accumulation of blood lactic acid with an increase in hydrogen ion concentration and a fall in plasma carbon dioxide combining power This was accompanied by a rise in blood sugar Morton, however, reported that intravenous injections of alkalies were without effect in human hyperpyrexia cases Bock and Dill have shown that heat prostration and death may occur before the acid-base equilibrium is seriously disturbed A fourth theory is that heat stroke is due to the exhaustion of the sweat glands Hearne, who studied several hundred cases of heat hyperpyrexia in Mesopotamia, reported that in every

cause the skin was hot and dry indicating suppression of sweating and heat loss by evaporation. The resulting rise of internal temperature, he believed brought about certain changes in the brain and other tissues responsible for the symptoms. The cause of the suppression of the sweat glands was attributed to previous hyperactivity leading to exhaustion. Leonard Hill also suggested that exhaustion of the sweat glands may be the prime factor in heat stroke. That the sweat glands are subject to partial exhaustion was shown by Whitehouse who reported a decrease in the amount of sweat with an increase in duration even when water was drunk. Furthermore heat stroke *usually* occurs most *frequently after* several days of an extreme heat wave. Hearne believes that the onset of heat stroke can be predicted by the appearance of a dry skin indicating suppression of perspiration and the accompanying increase in frequence of micturition, and that under such circumstances preventive cooling treatment can be successfully applied.

It seems quite probable that there is more than one factor involved in producing heat stroke but at any rate, the resulting rise in body temperature to a level incompatible with proper physiological functioning, is probably directly responsible for most of the symptoms.

CONCLUSION

In conclusion then it is evident that we are still a long way from understanding the physiological basis of the effects of work in extreme heat. From the clinical viewpoint, however at least we have made some progress in the past few years by the use of salt and sugar in the prevention and treatment of heat cramp. With the present interest in this problem, we are looking forward to further progress in this field.

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ANALYSIS OF FIVE HUNDRED INTRA-OCULAR STEEL INJURIES[1]

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IN an analysis of 500 steel injury cases, I have come to the conclusion that the making of the diagnosis offers the greatest difficulty, and at times is likewise fraught with danger. To my mind, the dangers of diagnosis far outshadow the operative procedure and the great or small amount of trouble or infection which often follows the entrance of steel in the eye.

At times diagnosis is very difficult to make, in fact the presence of steel in the eyeball may be entirely overlooked unless a careful history is obtained. In my cases I have found that, in the order named, the occupations of die setter, boring mill operator, general machinist, auto mechanic, blacksmith and handy man job, are the ones which show the greatest number of eye injury cases. Moreover, the specific instance or instances of injury and the detailed explanation of the injury are necessary. In several of my cases, men have had two to three seemingly minor traumas in the same day, thereby clouding the issue of the important one. Subjective symptoms appear to be of little worth in arriving at a conclusion, for the entrance of a small bit of steel in the eye is often absolutely painless and the patient may be totally unaware of an accident. In these cases most stress in the diagnosis must be placed on the objective findings. Visual tests offer little aid, as unless evident damage has been done, the vision may be normal to the cornea, lens, or iris. In 8 per cent of my series, the entrance wound was extremely small, necessitating a careful search to find it, and in at least half of this number of the cases, no external wound could be found as the injury was 2 to 3 days old. Therefore the diagnosis settles down to the examination of the deeper structures. I have found that fine floaters offer the best clew in these cases as they have been present in the greatest majority of them. Fine or pin point opacity in the lens at the periphery or elsewhere, is of great importance, whereas fine lesions in or about the retina or choroid seldom have been seen immediately following the injury.

The corneal microscope and slit lamp have been of great aid for fine wounds in the cornea or lens, but in certain types of cases, especially those of several days' duration, little aid is obtained. To me, therefore, the X-ray film has been the sheet anchor upon which to fall back. I have made its use a routine procedure in my practice, even when there seemed to be no definite indication, and the results have been surprising. By X-ray picture, I do not mean the film obtained at the average surgeon's office, as such plates are seldom of much value. For the diagnosis of intra-ocular steel, say 1/2 by 1/2 millimeter in size, it is often necessary to take 3 to 6 plates at different angles before a definite conclusion can be reached. In my series I have a case in which steel was overlooked by one good X-ray laboratory and found by another. It is evident therefore, that not only is the X-ray plate most important as a diagnostic aid but it is the best means of diagnosis obtainable. Exact localization is extremely difficult, and where 1/2 to 1 millimeter means so much, i.e., just in or outside the globe, its extreme importance is readily seen. After the steel has been properly localized—and this is often subject to variations as noted—the operative procedure to be used must be considered.

In my series, the selection of operation has been peculiarly influenced by the laws of my state and the surrounding states. Compensation laws differ, hence the mode of attack must conform in some degree with the economic side. In those cases with steel posterior to the lens and the lens uninjured, the posterior route was the one of choice, even with the danger of subsequent retinal detachment. In all cases in which the lens has been injured, the anterior route was used. It was found that a large operative opening for the magnet point was superior to one in which the point was difficult of entrance, as it entailed less danger of added trauma in the posterior opening. In practically all my cases, the patients were men direct from shops, hence dirty. As a routine procedure, installation of 2 per cent mercurochrome, followed by a thorough irrigation of the eye with 1/3000 bichloride was used. Moreover the mouth was examined for any evident foul, decayed teeth and, if possible, they were extracted at once.

In my early cases, boiled milk was used as a foreign protein, later typhoid serum, and now the hemo-protein of Parke Davis & Co., as the dose is smaller. I am unable to state with any degree of accuracy the effects of foreign protein injections, although I have used such a procedure as in all operative cases. In this series, I have had 32 cases in which the foreign body was not magnetic steel, or was magnetic steel in combination with some other substance such as rubber or bakelite. In

[1]Presented in the Symposium on Industrial Medicine and Traumatic Surgery, before the Clinical Congress of the American College of Surgeons, San Francisco, October 28–November 1, 1935.

several cases the foreign bodies were brass, copper zinc, and as many were bits of glass. In these cases, two factors appeared to be of most importance (1) the location of the foreign body (2) the amount of pure luck in its extraction. I might add that I have been blessed with my share. I have 2 cases of copper in the ciliary body for more than 10 years which have caused no trouble 3 of brass in the retina and sclera with no inflammatory symptoms and 2 cases with iron in the periphery of the lens, one 20 years old and the other 5 years old. No cataract has developed, as apparently the foreign body has acted as a bung in a barrel However when a definite diagnosis of intra-ocular foreign body has been made it has been my procedure to use any and all means that will extract the foreign body if iron or steel, but if of other substance the localization will decide the course to be pursued. I have found that the eye will stand a large amount of operative trauma at times with surprisingly good end-results

Complications of minor or major importance developed in over 88 per cent of my cases. In not quite 12 per cent, there was no reaction and no specific loss of vision. Just to what to attribute this in 12 per cent of the cases, is a mystery to me as they were varied types. Possibly the patient's own resistance, lack of infection carried in, or possibly lack of fault in my technique, furnish the explanation. Three patients developed sympathetic ophthalmia they all disregarded instructions to report at intervals for check up I have had 12 cases of beginning sympathetic irritation, which subsided promptly on enucleation of the offending eye and suitable medication I am therefore not in the dread fear of this complication that I was years ago for I believe that it can be readily handled if it develops while the patient is under observation One case of gas bacillus panophthalmitis secondary to steel injury had a favorable outcome following enucleation Detachment of the retina following steel extraction has been difficult to handle as with it other complications have arisen to increase the hazards of operative correction

The removal of traumatic cataract has been urged in the anterior route cases, and seldom has the swollen lens caused undue trouble following the injury

Detachment of the retina has occurred in approximately 14 per cent of those posterior operations in which the eyes were not enucleated The insurance companies are not prone to spend extra money for medical care for the correction of a detached retina, and in my state, Illinois, for traumatic cataract cases The insurance companies feel that the best results will not pay for the cash spent. In my state, many cases of traumatic cataract go about uncorrected for this reason, and what might be a good result is checked otherwise

TABLE I.—RESULTS

	Per cent
Panophthalmitis	13
Uveitis necessitating enucleation	14
Phthisis bulbi	4
Detached retina	14
Traumatic cataract with good prognosis	13
Fundi damaged including retina and choroid plus damage to lens	10
Those with final normal vision	3
Those with 75 vision	8
Those with 50 vision	20
Those with less	30

From the standpoint of good end results and of the operative procedure for intra-ocular steel injuries, I have come to the conclusion that industry would profit greatly if (1) employees teeth were given more care, (2) all patients with eye injuries of every description were sent to an oculist for diagnosis and treatment, (3) the compensation laws of all states were the same, (4) the employer was prevailed upon to handle the after complications.

In the analysis of my cases as to the pathology and vision, Table I shows a summary of results

The above record of the final results is anything but enviable, but there are several factors to be considered if better outcomes are to be assured The most important is prevention of injury The National Safety Council has for years waged a campaign along this line, and it has undoubtedly borne some fruit, but when the injury has taken place, its severity will determine to a great degree the final outcome. It appears to me then, that when the diagnosis of the presence, size and exact location of intra-ocular foreign body has been properly made, we have done the major part for our patient. The surgical side, depending as it does upon the location for complications, at this time does not offer much aid.

REPORT OF 1935 SURVEY OF MEDICAL SERVICES IN INDUSTRY BY THE AMERICAN COLLEGE OF SURGEONS[1]

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DURING the past year the medical services of 192 industrial organizations have been personally surveyed. To date the medical services of 1,314 establishments which serve 3,220,000 workers have been under survey by the American College of Surgeons. Of this number 708, or approximately 55 per cent, are approved by the College. This relatively high percentage does not mean that 55 per cent of all industrial medical services merit approval. It should be borne in mind that the surveys of the College have been directed principally toward the larger industrial organizations, in which the percentage of organized medical services is much higher than in the smaller establishments. Only a low percentage of the smaller firms have medical services that as yet merit approval, although it is gratifying to note the growing interest manifested by the smaller establishments in improving their organization for such service. This growing interest on the part of both large and small organizations, and their desire to receive approval from the American College of Surgeons has materially promoted co-operation and a closer working relationship between industry and the College.

TREND OF INJURY RATES

It is of interest to review recent experiences in the field of industrial medicine and traumatic surgery. From 1926 to 1934 there has been a reduction of 57 per cent in injury frequency rates, and a decrease of 37 per cent in severity rates, according to the National Safety Council report. The public utilities have made the most progress in reducing their injury rates.

The year 1934 shows an increase of 5 per cent in both frequency and severity rates over the year 1933. This is due to augmented industrial activity, wherein the new untrained workers, and the older employees who may have become careless in their work, were likely subjects for accidents. Furthermore, many safety and medical services were severely curtailed or allowed to disintegrate during the period of low industrial activity. A rather sharp increase in severity rates may be expected in some industries, when the time lost from occupational diseases, such as silicosis, is included in the compilations.

It is highly recommended that each industrial medical department compile an annual statistical summary, including its injury rates, its illness and injury experience and its costs. A comparison of such summaries from year to year will not only reveal the relative efficiency of the medical and safety services, but will also serve to uncover any existing weak points, and thus future objectives of the medical services will be indicated.

ACCIDENTAL DEATHS

The National Safety Council reports the number of accidental deaths in the United States for 1934 as shown in Table I.

SEVEN PRIMARY CAUSES OF DEATH IN THE UNITED STATES IN 1934

According to the information released by the Bureau of the Census, accidents, in the order of importance as a cause of death per 100,000 population, have moved from fifth place in 1933 to fourth place in 1934, as shown in Table II.

WORKMEN'S COMPENSATION LAWS

Since the scope and the extent of medical service in industry are greatly influenced by the Workmen's Compensation Laws, the trends and changes in the laws are worth considering.

Florida and South Carolina have enacted Workmen's Compensation Laws during 1935. North Carolina and West Virginia have made provisions in their laws to cover occupational diseases. New York has added "any and all occupational diseases" to its previous schedule of 27 diseases. The term "injury" has been held to cover some

TABLE I.—ACCIDENTAL DEATHS

	Number
Total	101,000
Motor vehicle	36,000
Home	34,500
Occupational	16,000
Other accidental causes	17,500
Disabling injuries	9,821,000
Wage loss, property damage, medical expense	$3,500,000,000

TABLE II.—PRIMARY CAUSES OF DEATH

1	Heart disease	240.2
2	Cancer	106.3
3	Nephritis	87.3
4.	Accidents	80.0
5	Pneumonia	79.6
6	Cerebral hemorrhage	76.8
7	Tuberculosis	56.5

[1]Presented in the Symposium on Industrial Medicine and Traumatic Surgery, before the Clinical Congress of the American College of Surgeons, San Francisco, October 8–November 1, 1935.

occupational diseases in Massachusetts and Oklahoma, so there are now 15 states and the District of Columbia in which occupational diseases are recognized, and compensation is awarded for the resultant disabilities.

The Workmen's Compensation Laws of Kentucky and West Virginia have elective provisions concerning silicosis. West Virginia has a medical board for the handling of silicosis, and Massachusetts has a division of occupational hygiene in the *Department of Labor and Industry* and a provision for industrial disease referees selected from a list compiled by the Board of Registration in Medicine California, Maryland, Michigan, and New Hampshire have appointed committees to study occupational diseases, although the committee in California is restricted to the study of silicosis only Undoubtedly specific legislation covering occupational diseases will ultimately follow these investigative studies.

As a result of the extension and amplification of the Workmen's Compensation Laws, which might be viewed as a broad sociological measure, and of the increasing manufacturing processes with attendant health hazards, added responsibility is being placed upon the employer As a consequence, more efficient function is being expected from the medical service, particularly in its preventive phase The following suggestions, therefore, which embody the working principles of the Minimum Standard, should be observed by all industrial medical services

1 A definitely organized plan for medical service
2 A definitely designated staff of qualified physicians, surgeons, and attendants
3 Adequate emergency dispensary hospital facilities
4 Pre employment and periodic physical examinations to be made only by a qualified medical examiner
5 Education of the employee in accident prevention and personal hygiene
6 Elimination or control of all health hazards
7 Adequate medical records, accurately filed in the medical department under medical supervision and responsibility
8 Supervision over the sanitation of the plant and all health measures, by the physician or surgeon in charge
9 An ethical and co-operative relationship with the private practitioners
10 The use of approved hospitals

Our surveys have revealed that better organization of the plan for medical service, a higher standard for physical examinations of employees *and records thereof, adequate medical supervision* of the service, and the elimination or control of health hazards, offer the greatest opportunity for advancement in the field of industrial medicine at the present time. This statement is made in full cognizance of the splendid progress that has occurred in accident prevention, in the control of infection, and in traumatic surgery but these advancements may be classified as accomplishments, while the former represent an existing need

A certificate of approval is granted to an industrial establishment in which the medical organization and service *is fully approved and is of such a* nature as to give reasonable assurance of continued compliance with the Minimum Standard This certificate which is similar to that for hospitals, has stimulated considerable interest among industrial executives. As a consequence, many industrial medical services have recently been reorganized and definitely improved in order to merit a certificate of approval from the American College of Surgeons. This response from industry is most gratifying In order that the certificate of approval may always be significant of "adequate care of the ill and injured in industry appropriate care will be exercised at all times to insure that such certificates are granted only to the industrial medical services that merit such recognition

OPHTHALMOLOGY AND OTOLARYNGOLOGY

SURGICAL CORRECTION OF DEFECTS DUE TO PARALYSIS OF MUSCLES OF THE EYES AND LIDS[1]

MEYER WIENER, M D , F A C S , St Louis, Missouri

THE century mark has not been reached since Diffenbach first announced that he had effected a cure in a case of convergent strabismus by dividing the internal rectus muscle In the middle of the eighteenth century, the charlatan John Taylor had effected cures by operation, but he evidently did not know himself just what was necessary in the technique, and carefully avoided giving out details as to his prodecure

Eye muscle operations developed gradually after that Aurand quoted Velpeau as having inaugurated the treatment for paralytic squint, followed by Guepin de Nantes, and later von Graefe, who formulated the indications in 1862 He concluded that correction of the right superior oblique is best done by tenotomy of the left inferior rectus Knapp was the first to advance the inferior rectus for paralysis of the superior oblique Eperon, in 1889, traced in historic detail the whole question and reported 6 successful cases in which patients were relieved by advancement of the inferior rectus on the same side Jackson advocated the more logical method of transplanting the superior rectus backward and outward Recently Aurand reported a case of diplopia due to paralysis of the superior oblique, completely relieved by transplanting the inferior half of the external rectus and the temporal half of the inferior rectus to a point 3 millimeters from the inferior temporal margin of the cornea This gives the pull downward and outward, exactly what the paralyzed oblique lacked The method, to me, seems more sound than any Wheeler advocated advancement of the superior oblique, especially for excessive elevation in adduction He admitted that the technique is not easy A simpler way of effecting a similar result, provided one wished to utilize the oblique, would be to expose the tendon between two hooks without cutting the superior rectus, and either resect or tuck the tendon This can be easily accomplished in 10 minutes' time with little trauma to the tissues

For paralysis of the sixth nerve Dransart transplanted the superior oblique to the attachment of the externus The same year Hummelsheim reported 2 successful cases of paralysis of the external rectus by transplanting a strip of tendon from the outer half of the superior and inferior recti to the insertion of the paralyzed externus tendon O'Connor greatly improved Hummelsheim's operation by transplanting the nasal halves of the vertical recti By leaving the temporal half attachment to help pull outward and taking away the nasal halves, reducing the pull inward, a considerable increase in abduction was secured Earlier, he had suggested utilizing a strip from the margin in suturing to the transplant, intended to lessen the tension Moncado transplanted the superior rectus to the tendon of the externus, and then took a strip of the internus and attached it to the insertion of the superior to replace the superior rectus

I am presenting a method which has given me even better results because of its simplicity and greater ease of accomplishment. The externus is exposed, split down the center, cut off about 15 millimeters from its attachment, and the upper half is sewed to the superior rectus tendon, the lower to the inferior In this manner, the sound tendons of the vertical recti are not unnecessarily mutilated By attaching to the nasal half of the vertical tendons, a greater effect can be gained One can always section the nasal portions of the vertical recti later if he wishes, but I have not found it necessary to do this When contracture has occurred in the opposing internus, a recession is made first

Third nerve paralysis is a most distressing deformity Jackson first suggested transplanting the tendon of the superior oblique to the insertion of the internus He had performed the operation on the cadaver, and had believed it would work He also suggested that the operation might be supplemented later by splitting the externus and attaching the upper half to the superior and the lower half to the inferior He expressed belief of the possibility, in a young person, of re-establishing a limited field of binocular fixation and stere-

[1]Presented before the Clinical Congress of the American College of Surgeons San Francisco October 28–November 1 1935

Fig 1 Scheme showing method of transplanting strips from paralyzed externus to tendons of superior and inferior recti

opsis Independent of this knowledge I performed this operation (20) with most satisfactory results. The superior oblique is very readily exposed subconjunctivally by first placing the hook under the superior rectus and feeling the resistance of its attachment just as though one were to work on it. Then reversing it without changing its location, and pulling in the opposite direction backward, the resistance of the oblique attachment is felt and its tendon pulled forward. After it is exposed between two hooks and stretched a Weber canaliculus knife is slid along, the tendon toward and into the pulley the cartilaginous pulley cut with a sawing motion, and the tendon is cut off to a suitable length and sewed to the sclera just above the insertion of the internus. This prevents upward torsion There is a tendency to leave the tendon too long, which was my early mistake The lid is raised by a modified Lever procedure, a strip of fascia lata being used as a hammock. An incision is made in the skin

Fig 2 First step in modified Lever operation. Two incisions have been made above brow and one in lid Reverdin needle is seen ready to draw strip of fascia up to first opening in brow

in the middle of the upper lid, thus exposing the tarsus and cleaning it of orbicularis. Two incisions are made above the brow down to the occipitofrontalis, one on either side A Reverdin needle is passed from one opening over the brow down, under the skin to the opening in the lid, the fascial strip is drawn up and the end is sewed to the occipitofrontalis tendon. The Reverdin needle is then passed from the other incision above the brow to the lid opening the strip of fascia is drawn up, a round toothpick having been first slipped through the loop of fascia to deter

Fig 3

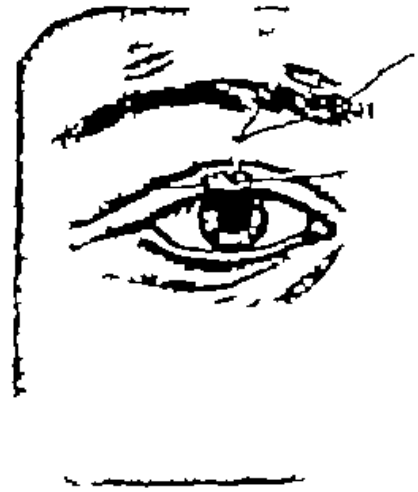

Fig 4

Fig 5

Fig 3 Second step in modified Lever operation Reverdin needle ready to draw up strip of fascia into second brow incision

Fig 4 Third step in modified Lever operation, showing how toothpick holds fascia strip in the desired position while sutures are being placed

Fig 5 Fourth step in modified Lever operation Final suture of fascia to tarsal plate

mine, by upward traction, where to anchor the strip end on the brow The strip is then fastened to the tarsus by two buried silk sutures

I recently had a case of congenital paralysis of the inferior rectus, with paralysis of the superior oblique and weakness of the internus and externus The inferior oblique seemed overactive I exposed the inferior oblique, cut it off about 12 millimeters from its attachment to the orbit, and sewed it to the sclera just to the nasal side of the paralyzed inferior rectus, and 4 millimeters closer to the cornea The newly transplanted muscle is beginning to function and there is a definite improvement in the patient s appearance The inferior oblique is easily exposed through a conjunctival incision in the lower cul-de-sac, a hook being introduced well to the temporal side of the insertion On drawing the hook nasally, the inferior wall of the orbit is hugged, the resistance of the attachment is met, and the tendon is pulled into the wound

In spasm of the inferior oblique, secondary to paralysis of the opposite superior rectus, McCool considers beneficial graduated tenotomy of the oblique made across the belly of the muscle

Fig 6 Shows how adhesive makes traction on cheek, bringing up the lower lid to cover the eye, with no pull on the sutures anchoring the upper to the rectus

McDanold transplanted the lower half of the externus and internus to the normal insertion of the inferior rectus in paralysis of the latter He also performed tenotomy of the superior rectus

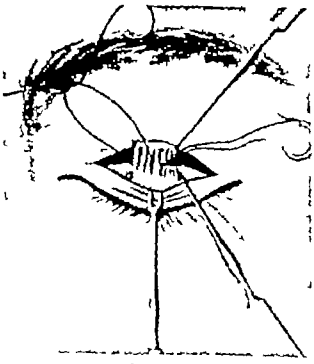

Fig 7

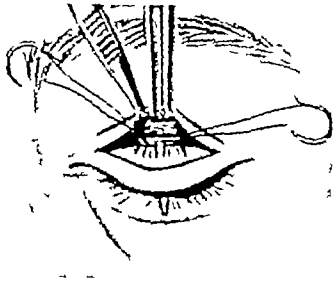

Fig 8

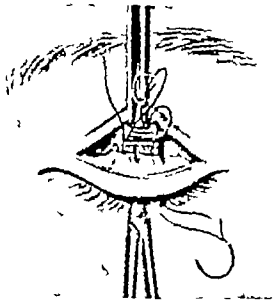

Fig 9

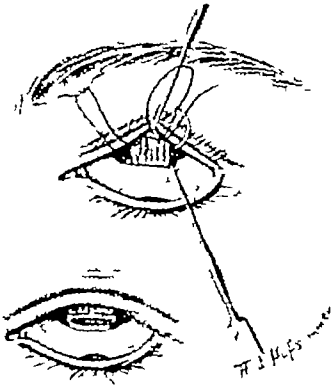

Fig 10

Fig 7 Scheme drawing showing the levator tendon grasped between two hooks and the sutures being put into position.

Fig 8 Levator tendon has been cut and opening is being made through the fascia and conjunctiva into the upper cul-de sac.

Fig 9 Suture being drawn into cul-de-sac.

Fig 10 Final suture to tendon of superior rectus

Fig 1. Scheme showing method of transplanting strips from paralyzed externus to tendons of superior and inferior recti

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Fig 2 *First step in modified Lexer operation* Two incisions have been made above brow and one in lid Reverdin needle is seen ready to draw strip of fascia up to first opening in brow

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Fig 3

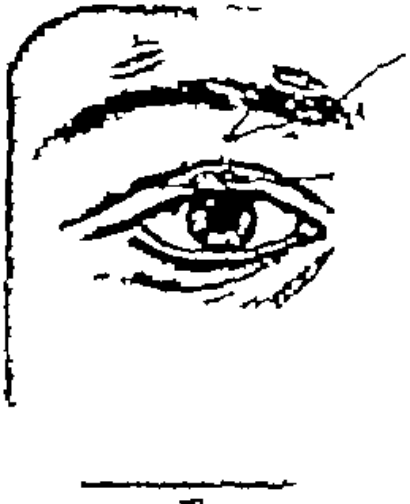

Fig 4

Fig 5

Fig 3 Second step in modified Lexer operation Reverdin needle ready to draw up strip of fascia into second brow incision

Fig 4 Third step in modified Lexer operation, showing how toothpick holds fascia strip in the desired position while sutures are being placed

Fig 5 Fourth step in modified Lexer operation Final suture of fascia to tarsal plate

Posey, Chance, and O'Connor performed similar operations

Operations for the relief of ptosis involve 3 principles

1 The folding, shortening, or advancement of the partially paralyzed levator This, in my experience, is not at all satisfactory

2 The utilization of the action of the occipito-frontalis muscle This is to be used when a sound superior rectus is not available The modified Lexer, with the fascia lata hammock, has given me the most satisfaction in this type of case

3 The utilization of the action of the superior rectus Motais, in 1897, first described this method of transplanting a strip of tendon from the superior rectus to the anterior surface of the tarsus Many modifications of this operation, all using the same principle, have been set forth Two years ago, before the American College of Surgeons in Chicago, I utilized Motais' principle, but reversed the procedure, attaching the paralyzed levator to the intact tendon of the superior rectus It has the advantage of being easier to perform and not so precarious as the original Motais operation In addition, it leaves no dent in the middle of the upper lid In reviewing the literature, I found that it had already been suggested by Cannas, and later by Arranquez If this method is carefully carried out, it hardly admits of failure The tarsus is exposed by an incision across the center of the upper lid near the upper border of the tarsus, the main portion of the levator near the tarsus is exposed between two hooks, two sutures are placed close to its insertion in the tarsus, and the levator then is cut off about 6 millimeters from its tarsal attachment A pocket is made, with a straight, blunt scissors, through the levator and fascia about 15 millimeters above the upper border of the tarsus and through the conjunctiva into the upper cul-de-sac The speculum is introduced, and the conjunctiva is dissected down to expose the superior rectus tendon, which is freed of capsular attachment The sutures are drawn into the upper cul-de-sac and sewed, one to each side of the superior rectus tendon about 5 millimeters back from its insertion Fine silk sutures are used No suture is required for closure of the conjunctival incision and only one skin suture is necessary in the lid The eye is protected with a light dressing by pulling up the lower lid by means of a broad piece of adhesive stretched from the cheek to the forehead which eliminates pull on the upper lid and effectively covers the globe No dressing is needed after 48 hours The adhesive strip is applied at night until the lid closes of itself

Two methods are recommended for sagging lower lid in the defect resulting from facial palsy A triangular piece can be excised from the temporal third of the lower lid with the lid margin forming the base and the apex down, deep sutures can be made, drawing the cut edges together, thus tightening the lower lid margin and bringing it flush with the globe Its effect is not altogether permanent but it is more satisfactory than anything else I have tried I have thought of using a different method on the next case, which I believe would be better A strip of fascia lata is anchored to the internal canthal ligament, it is run under the lid margin subcutaneously to the outer corner, and sewed, tightly stretched, to the external canthal ligament and periosteum of the outer orbital margin This, I believe, will hold the lower lid firmly against the globe and prevent the disagreeable constant flow of tears, as well as add greatly to the patient's looks

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MOTION PICTURE STUDY OF LARYNGEAL LESIONS[1]

FRANCIS E. LeJEUNE, M.D. New Orleans, Louisiana

THE motion picture film has been found of inestimable value in teaching the younger student clinical pathology of the larynx. Even in the larger clinics it is not always possible to have at hand the various types of laryngeal lesions for teaching purposes. To have an accurate record of a large variety of pathological cases for screen presentation is obviously advantageous not only for the teaching of the student, but also for the benefit of the general practitioner whose advice most of these patients seek early in their difficulty. Not only the general practitioner should be made to appreciate the importance of voice changes, but the public in general should be made to realize that persistent hoarseness is the danger signal of the larynx. Because the hoarseness which commonly complicates an ordinary cold subsides spontaneously most persons consider this symptom a trivial condition. Unfortunately however this is not always true. Any patient who has had a persistent hoarseness over a period of 10 days or 2 weeks should be given a thorough examination with the laryngeal mirror for it is only in this way that an early diagnosis can be made of tuberculosis, syphilis, carcinoma, and tumors of the larynx. The importance of an early diagnosis cannot be stressed too vigorously since many of these conditions in their early stages are amenable to treatment.

The most essential requisite in obtaining motion pictures of the vocal cords depicting various pathological conditions, is an adequate exposure of the structures of the larynx. This is best accomplished in my experience by the use of the suspension laryngoscope following the technique so ably described by Lynch (2). The use of the suspension laryngoscope is extremely simple and when properly employed gives a most excellent view of the laryngeal structures (Fig. 1). The hypopharynx, pyriform fossae and base of the tongue are likewise exposed to direct vision. This method permits the free use of both hands in all surgical procedures within the larynx. The tremendous advantage of such a procedure is obvious. The vocal cords can be retracted for subglottic examination by means of a retractor or a wooden spatula placed between the cords for abduction when cauterization or coagulation is necessary. Small tumors can be grasped and traction can be made to the opposite side in order to expose the base thus facilitating dissection. Punch forceps are not used when operating on these types of cases. My experience with them has been that an excess of scar tissue is formed in the healing process. I have obtained better results by grasping these smaller growths with fenestration forceps and, while making traction to the opposite side, carrying out sharp dissection with the laryngeal knife for the removal of the growth. Such a procedure usually insures a smooth, straight cord when healed.

Endolaryngeal surgery is simplified by the use of the suspension laryngoscope and, whereas benign growths are readily handled, malignant cases require more careful selection. Only the early intrinsic types of carcinoma are suitable for endolaryngeal surgery. These lesions are removed by dissection followed by coagulation. The results achieved are equally as brilliant as those reported by Lynch (3). Extensive malignant conditions require more radical methods. Whereas a few of the accompanying illustrations have been taken under local analgesia the vast majority of cases are given general anesthetics by choice. A combination of gas, oxygen and ether are used routinely except in those cases in which cauterization or coagulation is contemplated. For the past 3 years chloroform has been used exclusively when electrosurgical measures are considered. This procedure was adopted only after a tragic experience while coagulating a lesion on the vocal cord. A spark was accidentally created, there was a sudden explosion followed by an ignition of the ether fumes. The patient suffered severely from burns and shock and rapidly developed a pneumonic condition which proved fatal on the third day after operation. Chloroform is non-inflammable and non-explosive and is considered the only safe general anesthetic to use when the use of electrosurgical methods is considered.

In reviewing the lesions presented, attention must be called to the physiological function of the aryteno-epiglottic and false cords and the protection thus given the true vocal cords. The bechic action of the larynx and vocal cords in the expulsion of the tracheal secretion is most interesting to observe. The synchronous vibration on expiration demonstrates that any pathological condition existing on one or both cords must interfere with phonation.

Multiple papillomas of the larynx are by far the most common pathological lesions found in chil-

[1] Presented before the Clinical Congress of the American College of Surgeons, San Francisco, October 31–November 4, 1939.

Fig 1.

Fig 2

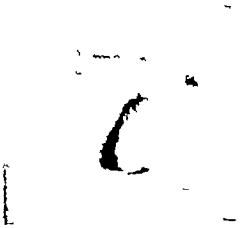

Fig 3

Fig 4.

Fig 5

Fig 6

Fig 7

Fig 8

Fig 1 View of a normal larynx
Fig 2 Papilloma growing from right vocal cord
Fig 3 Multiple papillomas on right vocal cord
Fig 4 Multiple papillomas completely filling laryngeal aperture
Fig 5 Papillomas of left vocal cord in adult.
Fig 6 Postoperative view of Figure 5
Fig 7 Vocal nodules on both cords
Fig 8 Postoperative view of Figure 7
Fig 9 Cystic fibroma attached to left vocal cord
Fig 10 Postoperative view of Figure 9

Fig 9

Fig 10

dren (Figs 2 and 3) The extent of the growth may vary from a small patch of papillomas to complete obliteration of the glottic chink by the growths (Fig 4) Removal of these growths under suspension laryngoscopy can be accomplished, but the problem of recurrence is one which has not as yet been solved Many cases of multiple papillomas are cured after the first or second removal from the larynx, and other cases, identical in every respect, defy every known method for their eradication During the past 2 years, following the removal of early cases of papilloma, we have used small doses of X-ray after operation as advocated by Foster While a few cases have responded satisfactorily, many other cases have recurred repeatedly regardless of the manner of removal or other therapy instituted Multiple papillomas respect no portion of the larynx, they will grow from any part, even from the subglottic region Much is yet to be learned about the successful treatment of these distressing conditions The clinical course of papillomas in adults (Figs 5 and 6) is apparently different from that observed in children They do not recur with the same rapidity or frequency as in children, however, the continued presence or recurrence of papillomas in adults is viewed with alarm and usually is considered as a precancerous lesion which should be watched for any malignant change

Vocal nodules (Figs 7 and 8) are the result of voice abuse and are seen in patients who persist in using an inflamed larynx or indulge in straining the voice The majority of such cases respond to vocal rest, but when this fails they become candidates for surgical removal Fibromas of the cystic type can become very large interfering considerably with phonation and respiration as shown in Figures 9 and 10 It is appalling that in this day and time of modern medicine, an intelligent individual should allow a growth in the larynx to reach such a size before seeking relief

Angiomas are frequently seen occurring on the vocal cords resulting from the too vigorous use of the voice with a rupture of a small vessel on the surface of the cord (Figs 11 and 12)

An early diagnosis in malignant conditions is imperative if intralaryngeal surgery is to be successful As stated above, only the earliest malignancies are amenable to intralaryngeal surgery While excellent exposure will facilitate the oper-

Fig 11

Fig 12

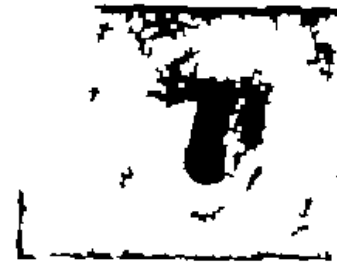

Fig. 13

Fig 14

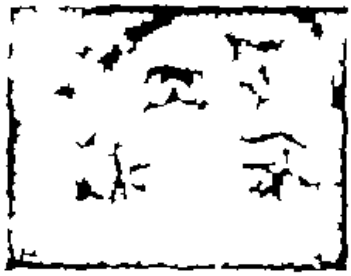

Fig 15

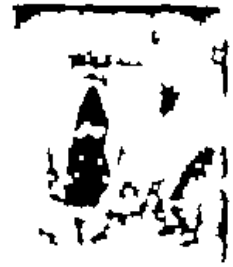

Fig 16

Fig 1 Angioma of anterior third of free border of right vocal cord

Fig 2. Postoperative view of Figure 1

Fig 13 Intrinsic carcinoma of right vocal cord

Fig 14 Carcinoma of mouth of esophagus and post cricoid region showing early infiltration of arytenoids and normal vocal cords

Fig 15 Supraglottic tumor carcinoma grade 3, attached to lateral surface aryepiglottic fold, larynx, and pyriform fossa

Fig 16 Postoperative view of Figure 15.

ative procedure the final results of endolaryngeal surgery are largely dependent upon the selection of the case and the thoroughness of the surgical removal. Three types of lesions are recognized *when endolaryngeal surgery is considered.* The earliest malignancies are those cordal lesions limited to the anterior and middle thirds of the vocal cords in which the growth is practically a surface lesion and consequently limited to the cells above the basilar membrane. The symptoms produced by such a lesion are, indeed, slight and *only mild voice changes are noted. The operative* procedure involves the resection of the growth with a free margin of uninvolved tissue on all sides Preservation of the vocal process which is possible only in early malignancies, is responsible for a good voice, when in due course of time, a pseudocord is formed In the second group are those in which the early lesion has extended with increased cell proliferation, induration, tumor size, and lagging of the vocal cord but without fixation. The lagging indicates that cell proliferation and growth have extended *sufficiently to involve* the muscle fibers but with no involvement of the joint. Complete extirpation of the cord followed by coagulation of the base is the only procedure that will give satisfactory results In addition to this, postoperative radiation is indicated. These patients are kept under observation for an *extended* period of time. Any recurrence will necessitate a second operative procedure, the type of operation depending upon the extent of the recurrence. A squamous cell carcinoma in a physician required three intralaryngeal operations to affect an apparent cure.

When Dr B first consulted us, mirror laryngoscopy showed an early carcinoma on the anterior third of the left vocal cord By means of suspension laryngoscopy the left vocal cord was extirpated from the vocal process to the anterior commissure and the base was coagulated. The *pathologist reported a squamous cell carcinoma grade* At the end of 4 months there was evidence at the site of the operation of small granuloma or else recurrence of the original lesion Surgical removal was accomplished with a more extensive electrocoagulation of the base. He was kept under close observation, and at the end of 10 months another small growth appeared in the region of the anterior third of the left cord This was again removed and cauterized The pathologist reported a squamous cell carcinoma *at the time of the second and third operations Four years* have elapsed since the last operation and only a hoarse voice produced by pseudocord remains as evidence of former trouble

To group 3 belong the border line cases (Fig 15), in which the extent of the lesion is such as to make the success of endolaryngeal surgery doubtful. The lesions in these cases are best removed through laryngofissure or preferably by laryngectomy Frequently a malignant lesion of the larynx is more extensive than the surface lesion *would at first indicate. In these cases,* there can be no compromise and radical surgery *is indicated.* We have always used the one stage operation and in the past 3 years, we have found that a straight midline incision has given even better *results than* the old T incision formerly used The straight incision is particularly of value in patients with thick necks. Retraction is easily accomplished and the larynx is dissected out with little difficulty *An* advantage is that it affords greater support in the reinforcement of the suture line in the plastic surgery performed *on the hypopharynx.* We have obtained primary healing in the plastic repair of

the hypopharynx in many cases since using this technique Proper selection of cases for laryngectomy gives good results and grateful patients

The complaint of a sensation of fullness or consciousness of the lower pharynx should never be dismissed without a careful examination, as malignant growths of the hypopharynx, pyriform fossa, and mouth of esophagus (Fig 14) give little warning of their presence until the lesion is far advanced Suspension laryngoscopy offers an excellent approach to these new-growths, but, unfortunately, in the majority of cases, little can be done from the standpoint of surgery

One case of supraglottic tumor with partial attachment in the pyriform fossa is illustrated (Fig 15) Dissection with complete removal was secured (Fig 16), and the patient is well without recurrence after a period of 3½ years This represents an unusually successful result because most malignant tumors of the hypopharynx are inoperable long before a surgeon is consulted The transhyoid and lateral pharyngotomy as advocated by Trotter is the best surgical approach to be used in treatment of malignancies of the hypopharynx The advent of radiation with its enormous possibilities and promises, offers more hope to these unfortunate individuals Martin has reported excellent results obtained by radiation in laryngeal and hypopharyngeal growths The one most important factor in the treatment of all these conditions is early diagnosis In cordal lesions, hoarseness is an early warning signal Hoarseness accompanying lesions of the false cords, aryepiglottic folds, and rim of the glottis is not an early symptom Lesions of the hypopharynx give little warning until far advanced Malignancies of the larynx could be cured more frequently if the public were conscious of the dangers attending prolonged hoarseness

While the black and white illustrations are of considerable interest, the exact reproduction of true colors existing within the normal and diseased larynx is the ultimate goal of motion picture photography In the past 2 years, success has attended my efforts directed at color photography so that today fully 600 feet of film showing pathological lesions are available in normal colors The recent production of a new color film promises to relegate to antiquity the former method employed in color photography Now more experimentation and time will be necessary to collect a sufficient number of cases to warrant presentation

Clinical experience is the method of choice in the teaching of clinical pathology of the larynx, and over a period of time all variety of cases can be observed A rapid review of all such cases is afforded in a few minutes by motion pictures While the laryngologist has ample opportunity to observe these various lesions in his practice, it is my ardent hope that these pictures will serve to stimulate the interest of the general surgeon in laryngeal conditions and to enhance the possibilities of an earlier diagnosis, particularly in malignant conditions Early diagnosis is imperative if one is to be successful in the fight against carcinoma of the larynx

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Fig 11

Fig. 12

Fig. 13

Fig 14

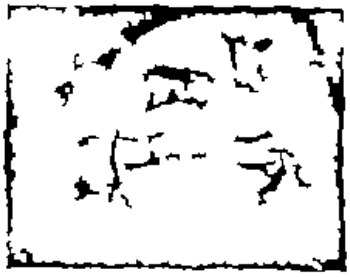

Fig 15.

Fig 16

Fig 11 Angioma of anterior third of free border of right vocal cord

Fig 12 Postoperative view of Figure 11

Fig 3 Intrinsic carcinoma of right vocal cord

Fig 4 Carcinoma of mouth of esophagus and post cricoid region showing early infiltration of arytenoids and normal vocal cords

Fig 15 Supraglottic tumor carcinoma grade 3 attached to lateral surface aryepiglottic fold, larynx, and pyriform fossa

Fig 16 Postoperative view of Figure 3

ative procedure the final results of endolaryngeal surgery are largely dependent upon the selection of the case and the thoroughness of the surgical removal. Three types of lesions are recognized when endolaryngeal surgery is considered. The earliest malignancies are those cordal lesions limited to the anterior and middle thirds of the vocal cords in which the growth is practically a surface lesion and consequently limited to the cells above the basilar membrane. The symptoms produced by such a lesion are, indeed, slight and only mild voice changes are noted. The operative procedure involves the resection of the growth with a free margin of uninvolved tissue on all sides. Preservation of the vocal process which is possible only in early malignancies, is responsible for a good voice, when in due course of time, a pseudocord is formed. In the second group are those in which the early lesion has extended with increased cell proliferation, induration, tumor size, and lagging of the vocal cord, but without fixation. The lagging indicates that cell proliferation and growth have extended sufficiently to involve the muscle fibers but with no involvement of the joint. Complete extirpation of the cord followed by coagulation of the base is the only procedure that will give satisfactory results. In addition to this, postoperative radiation is indicated. These patients are kept under observation for an extended period of time. Any recurrence will necessitate a second operative procedure the type of operation depending upon the extent of the recurrence. A squamous cell carcinoma in a physician required three intralaryngeal operations to affect an apparent cure.

When Dr B first consulted us, mirror laryngoscopy showed an early carcinoma on the anterior third of the left vocal cord. By means of suspension laryngoscopy the left vocal cord was extirpated from the vocal process to the anterior commissure and the base was coagulated. The pathologist reported squamous cell carcinoma grade 3. At the end of 4 months there was evidence at the site of the operation of small granuloma or else recurrence of the original lesion. Surgical removal was accomplished with a more extensive electrocoagulation of the base. He was kept under close observation, and at the end of 9 months another small growth appeared in the region of the anterior third of the left cord. This was again removed and cauterized. The pathologist reported a squamous cell carcinoma at the time of the second and third operations. Four years have elapsed since the last operation and only hoarse voice produced by a pseudocord remains as evidence of former trouble.

To group 3 belong the border line cases (Fig 13), in which the extent of the lesion is such as to make the success of endolaryngeal surgery doubtful. The lesions in these cases are best removed through laryngofissure or preferably by laryngectomy. Frequently a malignant lesion of the larynx is more extensive than the surface lesion would at first indicate. In these cases, there can be no compromise and radical surgery is indicated. We have always used the one stage operation and in the past 3 years, we have found that a straight midline incision has given even better results than the old T incision formerly used. The straight incision is particularly of value in patients with thick necks. Retraction is easily accomplished and the larynx is dissected out with little difficulty. An advantage is that it affords greater support in the reinforcement of the suture line in the plastic surgery performed on the hypopharynx. We have obtained primary healing in the plastic repair of

patient is allowed out of bed and general routine care is administered Atropine is instilled to keep the iris well dilated and metaphen solution (1 2500) is continued until the congestion which is present subsides

Although the trephine wound may filter, the conjunctival covering may become so thin that rupture and infection occasionally will occur Crushing the edges of the conjunctival wound, combined with suturing, produces complete closure which permits early, firm massage Ballooning of the conjunctiva and omission of the dressing also aids in maintaining drainage Complete closure of the wound reduces the danger of exogenous infection to a minimum and leads to early reformation of the anterior chamber which encourages normal drainage of the intra-ocular fluids and restoration of normal intra-ocular relations

IRIDOCORNEOSCLERECTOMY FOR GLAUCOMA[1]

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A TECHNIQUE for iridocorneosclerectomy is described which possibly combines the best features of the Lagrange iridosclerectomy, the Elliot trephine operation, and the Holth punch operation. The excision of tissue in the angles of the wound and the complete closure of the conjunctival wound over a bleb of salt solution usually produce a broad, evenly diffused, filtering cicatrix. The procedure seems to be indicated when a filtering operation is necessary, that is, in cases of chronic primary non-congestive glaucoma, in acute congestive glaucoma, in cases of secondary glaucoma, and in glaucoma following cataract extraction. Obviously cases with few secondary changes in the iris, early cases with minor field changes, and those in which miotics lower tension, react most favorably.

The contra-indications for iridocorneosclerectomy are the presence of advanced arteriosclerosis and unusually high blood pressure, new vessels on the iris, buphthalmos, and microphthalmos.

The technique is as follows: After aseptic preparation and injection of the eyelids, inject subconjunctivally over each rectus muscle 1 per cent procaine with 3 minims of a solution of adrenalin (1:1000) to each dram of procaine solution. In the operations performed recently, the ciliary ganglion was injected with 1 cubic centimeter of procaine adrenalin solution. The conjunctiva above the cornea is ballooned with the adrenalin novocain solution. With Stevens scissors, a slightly curved incision 15 millimeters in length, and 10 millimeters from the limbus, is made through the conjunctiva to the sclera with the concavity toward the cornea; this flap is dissected from the underlying sclera down to the cornea. The extremities of the incision should be kept at least 8 millimeters from the cornea. The flap is folded back over the cornea and dissection is done with a flat sharp spatula with a rounded end, gently into the layers of the cornea with a side to side movement. With a blunt spatula placed between the layers thus dissected and with the conjunctival flap restored to its original position, the point of the spatula should extend 1.5 millimeters into the cornea. The eye is directed and held downward with a fixation forceps, and an incision is made with a broad, hollow ground keratome. The incision is started in the sclera 1.5 millimeters above the limbus and is extended into the anterior chamber until a wound approximately 4 millimeters long is obtained. If the anterior chamber is shallow, the incision may be made with a short narrow curved Graefe knife. While the keratome is being withdrawn, care is exercised to prevent the iris from prolapsing into the wound. If prolapse occurs, and it cannot be replaced readily, exclude the iris with a spatula while the punch is being used. Stevens scissors are used to extend the angles of the scleral wound for a distance of 0.5 to 1.0 millimeter, which makes an incision approximately 5 millimeters long. The cuts should be parallel to the limbus and should allow the introduction of the special scleral punch into the angles of the wound. With the punch, the sclera and cornea (Fig. 1A) are clipped as deeply within each angle as possible; the remaining lip of sclera and cornea is then clipped, a serrated edge (Fig. 1B) being left. The wound should extend 0.5 to 0.7 millimeter into the cornea.

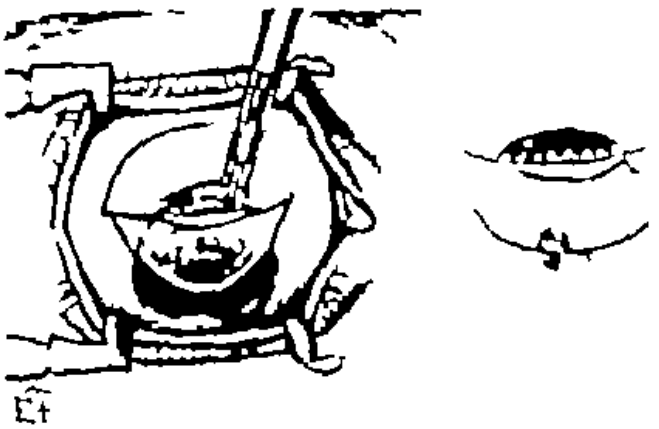

Fig. 1. A, left. Removal of the scleral and part of the corneal lip with special punch. B. Appearance of the wound uncompleted.

A broad tin cut glaucoma iridectomy is now performed. After the first cut, the iris is torn from the ciliary body by traction forward and toward the uncut side. In selected cases of chronic non-congestive glaucoma, a peripheral iridotomy or iridectomy may be performed.

The conjunctival wound is closed with an over and over running catgut suture (No. 0000 plain). After the suture is drawn tight and the wound edges, except at the extremities, are crushed with forceps, a grooved spatula is inserted in one angle as anterior chamber irrigator filled with half normal physiological saline solution is placed in the opposite angle, and all blood and fibrin are washed from under the flap. Sufficient solution should remain under the flap to balloon it forward and to restore the anterior chamber if possible. The extremities of the wound are now crushed and closed with forceps. Metaphen ointment (1:2500) is applied over the inner canthus, and 1 drop of 3 per cent atropine is instilled.

Since the ends of the suture have been cut close to the conjunctiva, a ring or a gauze mask may be applied over the wound without a dressing. The patient should remain in bed with his head elevated. In from 24 to 48 hours after operation, gentle massage of the eyeball is begun; this is repeated 3 times each day. On the day following operation, the

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MALIGNANCY OF THE UPPER RESPIRATORY TRACT AND ADJACENT STRUCTURES[1]

Selection of Treatment

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SELECTION of the most effective therapeutic agent for the treatment of malignant tumors of the upper respiratory and alimentary tracts is especially important because of the activity of the majority of these neoplasms. The institution of improper primary treatment is often responsible for a fatal termination later. Only a comparatively small group of therapeutic agents and procedures are worthy of consideration in the treatment of these tumors. Among these are straight surgical procedures, the actual cautery, escharotics, electrocoagulation, radium, and roentgenotherapy. Each of these possesses certain features which may be of decided value in a given case, but which may be of little value or even harmful, in another case. Choice of the proper agent or procedure is accordingly just as essential as is choice of the correct method of administration. The chief factors influencing such selection are the nature, situation, and extent of the lesion, whether or not it has been treated previously, and the age and general condition of the patient. Physicians are not entirely in agreement concerning the importance of these various factors, and conclusions based solely on personal experience at the Mayo Clinic are here presented.

In general, it may be said that treatment for neoplasms of the upper respiratory and alimentary tracts should never be instituted until a diagnosis has been established. This will frequently necessitate biopsy. The majority of malignant tumors of this region are squamous cell epitheliomas, and metastasis is prone to occur early. It accordingly is necessary to treat the regional lymphatics actively as well as to treat the primary growth. Wherever possible, surgical removal of the lymph nodes is most effective in preventing metastasis. In other cases, because of the extreme activity of the lesion, its situation, and the questionable prognosis, irradiation is preferable. Tumors that are situated in regions which are readily accessible may be excised or destroyed with the actual cautery or diathermy. Those that are situated in regions such as the nasopharynx or hypopharynx, difficult to reach, should be coagulated with diathermy or treated with radium or roentgen rays. Carcinomas of mixed tumor type, which are encapsulated, should be excised. Lesions previously treated, especially those which have been treated with irradiation, must be dealt with more radically than they were before, and the prognosis in these cases is, as a rule, less satisfactory.

Among the most important considerations in the selection of treatment for malignant lesions in this region are the nature of the tumor and its activity. While Broders' classification of malignant growths is not necessarily a criterion of their radiosensitivity, it is of considerable value in determining the type of treatment advisable in a given case and in anticipating the prognosis. Malignant lesions that have been graded 1, 2, or 3, if surgical, should be excised or destroyed with the actual cautery or electrocoagulation, and the regional lymphatic structures should be removed subsequently. This same procedure usually is carried out in the case of well localized epitheliomas that have been graded 4, and intensive irradiation is applied after operation. However, more reliance is placed on the radium and the roentgen rays. In the treatment of extensive lesions of moderate activity, irradiation can often be used advantageously to supplement surgical measures. Likewise, in dealing with highly malignant tumors, irradiation, which constitutes the major part of the treatment, may be applied to advantage following removal or destruction of all, or a portion, of the growth with electrocoagulation.

Because of the limited time, treatment of carcinoma of the lips will not be considered in this paper. However, the malignant lesions which develop on the inner surface of the cheeks correspond in their nature, activity, and clinical behavior to those which involve the lips, and the therapeutic indications are similar in the 2 groups. With few exceptions, the buccal lesions are squamous cell epitheliomas of slightly greater activity than those on the lip. Most of the buccal tumors are graded 2 or 3 according to Broders' classification. An occasional adenocarcinoma is encountered. Well localized growths situated on the anterior portion of the buccal surface may be excised with the cutting cautery, but destruc

[1] Presented before the Clinical Congress of the American College of Surgeons, San Francisco, October 28–November 1, 1935.

of 6 patients who had lymphosarcomas lived for 5 years after the operation

The majority of malignant tumors presenting in the nasal fossæ are the result of extension of neoplasms which originate in the maxillary sinuses, ethmoid cells, and nasopharynx However, a small group of malignant lesions develop primarily in the nasal fossæ Most commonly encountered are squamous cell epitheliomas, adenocarcinomas, lymphosarcomas, and fibrosarcomas Many of these are highly malignant In the selection of treatment, the nature of the tumor, its situation and extent, and the general condition of the patient must be taken into consideration Electrocoagulation and radium are most useful in this regard They may be applied directly through the nasal meatus or following lateral rhinotomy Since the Moure operation, i e , lateral rhinotomy, gives easy access and a good view of the tumor, and leaves a comparatively inconspicuous scar, it is usually preferable, unless the growth is small and situated anteriorly Thorough electrocoagulation can be carried out and radium points can be implanted as a supplementary measure When both the antrum and the nasal fossa are involved, the Denker operation furnishes a more satisfactory approach While, as a rule, there is little immediate reaction to even extensive electrocoagulation within the nasal fossa, great care must be exercised in the destruction of tumors situated high up, because of the possibility of burning through the cribriform plate with production of meningitis In a recent case in which an adenocarcinoma originated in the ethmoid cells and involved the frontal sinus and upper part of the nasal fossa secondarily, the tumor was approached through a semilunar incision along the inner border of the orbit The encapsulated upper portion of the tumor had produced pressure absorption of the posterior wall of the frontal sinus and exposed a portion of the dura which was approximately 1 5 centimeters in diameter When the tumor in the nose is extensive and highly malignant, implantation of radium points, together with radium packs or roentgenotherapy, will usually offer marked palliation However, active neoplasms that fill a large part of the nasal fossa and appear too extensive for operation, often will be found attached by only a small pedicle, and careful electrocoagulation and wide destruction of the attachment of this pedicle will result in a cure In the treatment of this group of tumors as well as those of practically all other portions of the upper part of the respiratory tract, with the exception of the larynx, intratracheal anesthesia is of decided advantage

Malignant tumors of the nasopharynx occur more frequently than is generally supposed The majority of these tumors are highly active squamous cell epitheliomas and lymphosarcomas While they may develop in any part of the nasopharynx, they most commonly originate in, or adjacent to, the fossa of Rosenmueller Here, they are in close proximity to a number of important structures and, through involvement of these, produce a characteristic symptom complex

Because of the activity of those tumors, the difficulty of accurately determining their extent, their tendency to metastasize early, and their inaccessibility, irradiation is the treatment of choice Roentgenotherapy or radium packs are used externally over the head and neck, and radium tubes on a pliable applicator are placed directly in contact with the tumor in the nasopharynx Operation is rarely indicated in this group of neoplasms, either for removal of the primary lesion or the regional lymphatics Palliation only is likely to be obtained, although the growth can often be held in check and the patient kept in comparative comfort for several years In a few instances, complete arrest of the disease for 6 and 7 years has resulted

The malignant tumors of the base of the tongue and hypopharynx are chiefly highly malignant squamous cell epitheliomas, lymphosarcomas, and adenocarcinomas Irradiation is the treatment of choice in the majority of these cases, for the same reasons mentioned in connection with neoplasms of the nasopharynx As a rule, implantation of radon or radium element points in the primary lesion is preferable to the direct application of radium tubes to its surface, because of greater accuracy and efficiency of the former Infrequently, tumors on the base of the tongue are encountered sufficiently early to justify electrocoagulation following exposure with modified laryngeal suspension This treatment is supplemented with implantation of radium points, and if the degree of malignancy is not too great, block dissection of the lymphatic structures on the same side of the neck is advisable A number of 5 year and even 10 year cures have been secured in this group, with both the irradiation and surgical measures which have been outlined

The great majority of malignant tumors of the larynx are squamous cell epitheliomas In general, they are best treated with radical operation, as only through an open operation can the majority of them be clearly visualized and rendered accessible At times, however, the nature, activity, situation, and extent of the lesion, or the age and general condition of the patient, render radi-

delayed. This is far preferable to prolonged observation. A considerable proportion of patients with carcinoma of the tongue also present a positive serological test for syphilis. This frequently leads to a great deal of delay in diagnosis and treatment, as antisyphilitic measures are usually instituted and the patient is kept under observation for a prolonged period, in spite of progression of the neoplasm. By the time the conclusion is obvious that syphilis is not responsible for the tumor the growth is often so hopelessly advanced that treatment is of no avail.

Malignant lesions of the tongue, if operable, may be excised with the scalpel or with some form of cautery knife. Often, radon seeds are inserted into the open wound prior to suturing. Closure of the wound following excision with the scalpel or with the cutting cautery is usually followed by primary healing. If the growth in the tongue is extensive or if the floor of the mouth is involved, surgical diathermy is, as a rule, preferable to excision. The former procedure is bloodless, although there is a possibility of secondary hemorrhage on separation of the slough. Radon seeds are frequently used subsequent to destruction by diathermy, especially in the case of active lesions. Carcinoma of the tongue which is not surgical is best treated with gold radon seeds or platinum points containing radium element. Some of these lesions respond remarkably well to this type of treatment, and in some instances growths that had appeared to be beyond help with any therapeutic measures have been cured. Besides local treatment of these extensive growths, external irradiation is applied over the regional lymph nodes. In cases in which treatment is surgical, bilateral dissection of the submental and submaxillary lymph nodes and block dissection of the lymph nodes on the side involved, should be carried out as soon as the condition of the wound in the tongue permits and the patient's general condition warrants. If the patient is not a good surgical risk, more conservative dissection of the lymph nodes should be carried out. Radium is at times implanted into the wound at operation, and intensive external irradiation is administered subsequently when extension to the lymph nodes is demonstrated. A total of 162 patients with epithelioma of the tongue were treated at the clinic. Of the 156 who were traced, 37.2 per cent were living 5 years after operation. Of 74 patients in this group who had no evidence of involvement of the lymph nodes, 51.4 per cent were living 5 years or more after operation.

Tumors of the pharynx and tonsils are, in general, highly malignant epitheliomas and lymphosarcomas. A small percentage are mixed tumors, sarcomas of special type, and epitheliomas which have a low grade of malignancy. Any of these neoplasms may be primary in the tonsils or in the adjacent tissues. It is often difficult to determine definitely regarding the primary site of origin. However the treatment is much the same for either group. The inactive epitheliomas should be destroyed with diathermy and radon seeds should be immediately inserted into the coagulated region. The regional lymph nodes then should be removed and the procedure supplemented by surface irradiation. In the case of active lesions, radon seeds are sometimes implanted in the affected nodes, directly through the intact skin or following surgical exposure of such lymph nodes. Highly malignant epitheliomas and lymphosarcomas are most satisfactorily treated with radium inserted directly into the growth or applied over its surface; radium packs or deep roent genotherapy may be used externally.

Many of these patients do very well, particularly if the lymphosarcomas are of a fulminating type and have been present for only a few weeks. Fibrosarcomas may be treated in the same manner although the response to treatment is, as a rule, less satisfactory than in the lymphosarcomas. Mixed tumors in this region are entirely different from the growths just mentioned. They are encapsulated, grow slowly and do not ulcerate or infiltrate the surrounding tissues until late in the course of the disease. Metastasis does not occur until their retaining capsule has been ruptured. Such tumors should be removed surgically either through the mouth or by external incision. Preliminary ligation of the external carotid artery on the same side renders the operation much easier and safer. Treatment of the lymph nodes is not necessary and the prognosis is good. Radium is placed directly into the wound if there is any question regarding the clean removal of the growth, and radium or deep roent genotherapy later is applied externally. If infiltration of the surrounding tissues has occurred, radon seeds and external irradiation will accomplish more than will surgical procedures.

The outlook in treatment of malignant tumors of the pharynx and tonsil varies with the type of neoplasm. Of 44 patients who were traced at the clinic following such therapeutic measures, 57.9 per cent were living 5 years or more after the treatment. Twenty-nine of the patients in this group had had adenocarcinoma of mixed tumor type, and 93.5 per cent of these were well whereas, only 26.5 per cent of the 9 patients who had squamous cell epitheliomas and 54.5 per cent

ORBITAL ABSCESS WITH COMPLETE RECOVERY[1]

DWIGHT C ORCUTT, M D, F.A.C S, CHICAGO, ILLINOIS

THE general impression that the oculist meets only with the simple, easily handled case and that when a serious complication is met he refers the patient elsewhere, is erroneous This misconception is probably due to the fact that we are inclined not to report cases of a grave nature, but more likely to lay stress on interesting operations and brilliant results

After surveying the operative field, I concluded that, inasmuch as cataract operations with their flaps and bridges, muscle operations with their tucks and recessions, operations for glaucoma with trephine, deep iridectomies, iridotases, and every means of establishing drainage, had all been discussed and rediscussed, some other topic would be of greater interest My investigation turned to other channels, my first thought was that I might discuss postoperative complications, unexpected drug reactions, or infections of a secondary nature, but finally I recalled that my most anxious moments had been spent over abscess of the orbit and surrounding tissues and so chose this for my topic

Orbital inflammation, cellulitis, phlegmon—of cavernous, cerebral, and systemic involvement—easily can be classed as the most severe conditions with which the oculist has to cope They require prompt and constant attention, treatment necessary to ameliorate the attending symptoms as well as the disease, and all directed toward the etiological factor Literature teems with the reports of cases of ocular cavernous and brain complications, most of which had unfavorable endings, few are reported with complete recovery and normal vision I have found the condition very hard to deal with, and for this reason I hope that my study will stimulate others to report not only the unfavorable but the favorable results

The etiological factors are similar to those of infections in any other part of the body, but when we bear in mind the close proximity of the orbit to the vital structures of the head, we readily realize the added importance of being able to determine the causative factor The nasal sinuses are the ones most frequently involved Infections may be present in the surrounding tissue, for instance, there may be operative complications, meibomian cysts may be present, or there may be encapsulated cysts The least common causative factor is metastasis It should be borne in mind that in treating these patients every effort should be made to determine the cause of the trouble

Symptoms of cellulitis of the orbit are, first, a feeling of discomfort with little or no visible inflammation soon the lids become edematous with the conjunctiva chemotic, mobility of the globe is impeded and proptosis begins, vision is blurred in proportion to the pressure and pulling on the optic nerve At this time there is a slight engorgement of retinal veins and possibly a swollen disc Severity of symptoms increases rapidly, with pain, rise in temperature, and possibly cerebral disturbance Perhaps the most important diagnostic point is the amount of retinal vein engorgement when this is great, cavernous sinus involvement is feared, when slight, the inflammation is confined to the orbital walls

Under constant treatment the infection may be arrested and the globe slowly may return to normal position When suppuration occurs, the edematous tissue reddens and the conjunctiva changes from a pale chemosis to an angry red, which indicates immediate surgical interference Incisions should be made fearlessly within the lid margins if possible, if this is impossible, then through the lids at the points showing the greater tension The knife is carried deeply into the orbital cavity being held close to the wall and between the muscle attachments More than one point of drainage is usually necessary, possibly a narrow wick drainage being inserted deeply in the wound and changed as the condition indicates The moment drainage is free, recovery is rapid The cornea is in great danger and should be watched carefully, for I know of no ocular condition that calls for more gentle care Only when the lids become flaccid, can we begin to lessen our vigilance Let me again repeat the warning of prompt and early incision before rupture has occurred Constant attendance, changing hot dressings, sustaining and symptomatic treatment, all are most important

I have probably had my share of inflammatory conditions of the orbit in my clinical work and will mention them briefly in connection with other cases gleaned from the literature A few of these had favorable endings, but in more the results were unfavorable, some even fatal. From my private records I have selected 3 cases of the most severe type in which the patients made a

[1] This paper is primarily intended to report orbital phlegmon with complete recovery but to perfect the review of so serious a condition I have included from literature, cases showing every phase of the disease namely favorable recovery unfavorable recovery and fatal termination Presented before the Clinical Congress of the American College of Surgeons San Francisco, October 28–November 1 1915

cal surgical measures inadvisable. Growths situated in the supraglottic region, especially those *springing from the epiglottis, are commonly inactive* in type, and at times may be destroyed readily with diathermy by using direct, indirect, or suspension laryngoscopy The prognosis in these cases is good. Pharyngotomy however is the most universally satisfactory method of dealing with the majority of the lesions in this region. Tumors which involve the epiglottis and extend posteriorly along the aryepiglottic folds and laterally into the pyriform fossae, are better taken care of through a subhyoid approach by making a transverse incision at the base of the tongue and drawing the epiglottis out into the wound. On the other hand, when there is limited involvement of one aryepiglottic fold with extension onto its outer aspect, or when there is involvement of the epiglottis and base of the tongue lateral pharyngotomy is preferable after removal of the thyroid ala and, if necessary, a portion of the hyoid bone In cases in which the growths are extensive preliminary tracheotomy greatly lessens the risk of pharyngotomy as in other laryngeal procedures.

Laryngofissure or thyrotomy is indicated in cases of laryngeal carcinoma in which the tumor is inactive and freely movable, but if the tumor is active it must be found very early and be well localized. After the larynx is opened in or adjacent to the midline, the lesion is destroyed with electrocoagulation, or is excised and the wound cauterized. The *results* as regards control of the malignant process are extremely satisfactory with laryngofissure in properly selected cases. Of 34 patients who have been traced following removal of laryngeal carcinoma in this manner at the clinic, 28 (82.3 per cent) were living and well 5 years after the operation.

When the malignant process involves both sides of the larynx or extends to the arytenoid cartilages on one or both sides, especially if it is active or if there is fixation, complete removal of the *larynx alone offers* a reasonable chance of controlling the disease. The operation has been perfected during the course of years until at the present the mortality following it is very low It is best carried out under cervical block anesthesia. While it may be done in a single stage, preliminary tracheotomy lessens the risk. Even though most laryngeal carcinomas are highly malignant, the operation will result in cure in a large percentage of cases, provided the tumor has not spread beyond the larynx. Seventy-three patients were traced following laryngectomy at the clinic, and 41 (56.1 per cent) of them were alive and well 5 years after the operation. These patients are routinely provided with a simple mechanical means of voice production, and most of them are able to resume their original calling

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THE general impression that the oculist meets only with the simple, easily handled case and that when a serious complication is met he refers the patient elsewhere, is erroneous This misconception is probably due to the fact that we are inclined not to report cases of a grave nature, but more likely to lay stress on interesting operations and brilliant results

After surveying the operative field, I concluded that, inasmuch as cataract operations with their flaps and bridges, muscle operations with their tucks and recessions, operations for glaucoma with trephine, deep iridectomies, iridotases, and every means of establishing drainage, had all been discussed and rediscussed, some other topic would be of greater interest. My investigation turned to other channels, my first thought was that I might discuss postoperative complications, unexpected drug reactions, or infections of a secondary nature, but finally I recalled that my most anxious moments had been spent over abscess of the orbit and surrounding tissues and so chose this for my topic

Orbital inflammation, cellulitis, phlegmon—of cavernous, cerebral, and systemic involvement—easily can be classed as the most severe conditions with which the oculist has to cope They require prompt and constant attention, treatment necessary to ameliorate the attending symptoms as well as the disease, and all directed toward the etiological factor Literature teems with the reports of cases of ocular cavernous and brain complications, most of which had unfavorable endings, few are reported with complete recovery and normal vision I have found the condition very hard to deal with, and for this reason I hope that my study will stimulate others to report not only the unfavorable but the favorable results

The etiological factors are similar to those of infections in any other part of the body, but when we bear in mind the close proximity of the orbit to the vital structures of the head, we readily realize the added importance of being able to determine the causative factor The nasal sinuses are the ones most frequently involved Infections may be present in the surrounding tissue, for instance, there may be operative complications, meibomian cysts may be present, or there may be encapsulated cysts The least common causative factor is metastasis It should be borne in mind that in treating these patients every effort should be made to determine the cause of the trouble

Symptoms of cellulitis of the orbit are, first, a feeling of discomfort with little or no visible inflammation, soon the lids become edematous with the conjunctiva chemotic, mobility of the globe is impeded and proptosis begins, vision is blurred in proportion to the pressure and pulling on the optic nerve At this time there is a slight engorgement of retinal veins and possibly a swollen disc Severity of symptoms increases rapidly, with pain, rise in temperature, and possibly cerebral disturbance Perhaps the most important diagnostic point is the amount of retinal vein engorgement, when this is great, cavernous sinus involvement is feared, when slight, the inflammation is confined to the orbital walls

Under constant treatment the infection may be arrested and the globe slowly may return to normal position When suppuration occurs, the edematous tissue reddens and the conjunctiva changes from a pale chemosis to an angry red, which indicates immediate surgical interference Incisions should be made fearlessly within the lid margins if possible, if this is impossible, then through the lids at the points showing the greater tension The knife is carried deeply into the orbital cavity being held close to the wall and between the muscle attachments More than one point of drainage is usually necessary, possibly a narrow wick drainage being inserted deeply in the wound and changed as the condition indicates The moment drainage is free, recovery is rapid The cornea is in great danger and should be watched carefully, for I know of no ocular condition that calls for more gentle care Only when the lids become flaccid, can we begin to lessen our vigilance Let me again repeat the warning of prompt and early incision before rupture has occurred Constant attendance, changing hot dressings, sustaining and symptomatic treatment, all are most important

I have probably had my share of inflammatory conditions of the orbit in my clinical work and will mention them briefly in connection with other cases gleaned from the literature. A few of these had favorable endings, but in more the results were unfavorable, some even fatal From my private records I have selected 3 cases of the most severe type in which the patients made a

[1]This paper is primarily intended to report orbital phlegmon with complete recovery but to perfect the review of so serious a condition I have included from literature, cases showing every phase of the disease, namely favorable recovery unfavorable recovery, and fatal termination Presented before the Clinical Congress of the American College of Surgeons, San Francisco, October 28–November 1, 1935

perfect recovery without deformity or lowering of the vision. All had severe general reactions, high temperatures, and malaise but the blood cultures were positive in but one.

REPORT OF MY THREE CASES

CASE 1 1915 Female, aged 32 years, married Following a severe nasal infection patient noticed irritation in the inner canthus of the left eye which rapidly increased I saw her days after onset when the globe was moderately proptosed lids, chemotic conjunctiva, edematous Vision was blurred and somewhat lowered Treatment was directed toward the nasal condition All cavities proved negative but the ethmoid Treatment at first was by means of suction and pack, but this condition steadily became worse and the temperature was over 101 degrees The ethmoids were cauterized without effect. The nasal local applications were used and care was taken to protect the globe After 4 days an incision was made deep into the orbital cavity at the inner canthus free drainage to pus was thus established The staphylococcus was found Symptoms began to abate and temperature dropped to normal Recovery was uneventful with vision of 20-20 Duration of illness about 3 weeks

CASE 2 Male, aged 50, married Patient was a very nervous individual The left upper lid had been swollen several days before I saw him I found a badly inflamed eye, marked edema, swollen lids which were very painful Temperature was 100 degrees Fahrenheit. He was unable to get satisfactory vision because of the swollen condition of the lids and conjunctiva An abscess of the upper lid was incised and cleansed Constant local and symptomatic treatment was instituted On the following day the symptoms were more marked temperature was 102 degrees and a septic condition was very evident. He was sent to the hospital We made 3 deep orbital incisions Pus appeared in all three and from this time, symptoms began to abate Three weeks elapsed the corneas remained clear and recovery was perfect Vision was 20-20

CASE 3 Female, aged 40 years, married A small tumor of 3 or 4 months' duration was removed It was located on the left upper lid, just below the brow The tumor was about the size of a pea, apparently encapsulated, lipoma like in character with cystic degeneration No laboratory diagnosis was made, as to all appearances it was simple cystic tumor The usual procedure was followed and the patient was sent home The following morning she came in with a septic condition and temperature of 103 degrees Fahrenheit The stitches were removed and wound was cleansed She was sent to the hospital, her temperature rose steadily to 105 degrees that evening The first laboratory reports indicated possible tetanus, so an injection of antitetanus serum was given Later in the evening laboratory analysis showed pure streptococcus infection, so vaccine for that was given Going more fully into the etiology the patient recalled that a small tumor followed a severe streptococcus throat infection about 6 months before As drainage was present from the tumor site, no further drainage was made at the time but moist dressings were constantly applied and symptomatic treatment instituted Vaccine gradually increasing from cubic centimeter was given at the low temperature wave On the third day following admission, an erysipelas condition began on the left side of face extending across the nose and finally involving both cheeks and brow The globe proptosed, conjunctiva was edematous, but the corneas remained clear, although vision was blurred Blood culture was positive for the streptococcus white count at one time was 29,000 The patient's mind became confused and her condition was grave Early on the third day a deep orbital incision was made through the lids externally and pus appeared Symptoms began to subside but increased again on the fifth day An incision at inner canthus again elicited pus A chill on the sixth day followed by rapid elevation of temperature called for a third incision Following this procedure, the symptoms gradually subsided and the patient left the hospital after 4 weeks with no deformity normal vision, *and full ocular movement*

The etiological factor in this case was directly traceable to a septic streptococcus throat infection *about 6 months previously* Patient distinctly recalled that the tumor began as a painful lump soon after and the inference was that it became an encysted streptococcus sac.

Treatment in general was the same in the 3 cases constant moist hot applications Vaccine was used in Cases 2 and 3, but the first used only the hot applications, wick drainage and symptomatic treatment the condition being secondary to a nasal infection.

ORBITAL CONDITIONS WITH EXOPHTHALMOS

On my service at the Illinois Charitable Eye and Ear Infirmary over a period of many years, we have of course met many cases of greater or less severity Some of the least severe have been orbital cellulitis or periostitis cases showing marked proptosis, edema, pain, retarded mobility of the globe, and disturbance of vision but, at no time, any of the most marked symptoms of suppuration. Under diligent treatment, both medicinal and local, the patients have recovered. In 2 cases I recall that the vision was greatly lowered and in 1 patient mobility of the globe lessened due to the long continued inflammation involving the ocular muscles.

We are seldom called upon to do enucleations In fact, from the reports of the various large hospitals, 1 2 or 3 enucleations are as many as are done in 1 year

Two orbital abscess cases with cavernous sinus involvement terminated fatally one in an adult and the other in a child upon whom a muscle operation had been performed. *This was in the* early days of catgut tucks and unquestionably was due to that.

We have also had 2 cases of tumor in which the diagnosis *was long in doubt*. In one, a tumor mass was found to be deeply to the outer and lower part of the orbit A biopsy proved it to be sarcoma A tumor about 10 by 20 millimeters *was removed* with a small part of the maxillary bone The globe returned to normal position and vision returned to 20-70, but the outward move-

ment was impeded, no doubt due to injury to the muscle during the rather extensive operation Three years have elapsed with no recurrence

We had a most interesting case of aneurism of the ophthalmic vein, extending deeply into the orbit and upward on the forehead to the hair line Proptosis was extreme, becoming an unsightly popeye Vision was reduced until the patient could move around only with the aid of the sense of touch A deep incision was made to the nasal and frontal area, and the largely distended vessel was ligated The patient showed marked improvement. A second ligation of branches terminated in a complete recovery and return of useful vision for this patient The dangers of a carotid ligation caused us to consider the milder method which proved eminently satisfactory The aneurism was caused by an automobile accident, the temporal walls as well as the orbital walls being fractured, but with not much displacement

It is surprising how few cases involving the orbit we see in the large clinics and, in reviewing the literature, I conclude this is general

While most of my patients were adults from 25 to 50 years of age, still the condition probably has occurred most often in children under 10 years of age A series reported by Gamble,[1] of the Children's Memorial Hospital, indicated that the majority recover without operative interference and that, in a surprisingly high percentage, vision is only temporarily disturbed, no doubt due to the greater resistance in childhood

The danger of orbital infections is increased because the infection probably begins under the very thin periosteum which is firmly attached to the sutures Infection may extend not only into the orbital contents, but also directly to the more dangerous area I am satisfied that recovery in the 3 principal cases reported, was due to early and extensive drainage, I can therefore earnestly urge surgical interference at the earliest moment the diagnosis is definitely determined Because the upper portion of the orbit is very thin and of course lies close to the brain and cavernous sinus, it should be avoided as much as possible in making the deep incisions So I repeat, confine the puncture to the internal and external angles, through the conjunctiva if possible, but if swelling is too great, the puncture must be made through the skin at the orbital margin This was necessary in 1 case, but in the 2 others the conjunctival incision was possible

OTHER CASE REPORTS

CASE 1 Dr O B Nugent, Chicago, Illinois Retrobulbar abscess with complete recovery Male, aged 37 years Patient had had marked swelling of left eye for 10 days, lids could be opened only by force Hot applications were used An incision was made through the upper lid at junction of the middle and outer thirds Much pus was obtained and drain was placed Discharge was profuse for about 3 days after which it gradually subsided Wound healed in about 10 days Swelling and edema did not entirely disappear for about 6 weeks Vision returned to normal

CASE 2 Dr Frank A Plum, Honolulu Northwest Med 1931 Aug Bilateral orbital abscesses, simulating cavernous sinus thrombosis Trouble started from pimples about the nose, both eyes were involved Symptoms of cellulitis were severe and simulated cavernous sinus Both orbital cavities were drained, also the frontal sinuses Vision was normal in left eye nil in right

CASE 3 Dr W F Scott Moncreiff Canadian M J, 1930 Aug Dacryocystitis leading to orbital phlegmon, optic neuritis and atrophy Female, aged 45 years, had an orbital abscess extending from the lachrymal sac There was severe ocular disturbance Symptoms gradually subsided after incision and later extirpation of the sac, but vision was lost, due to an embolism of the central artery Temperature ranged to 100 degrees Fahrenheit

CASE 4 Dr Paul L Mahoney, Little Rock, Arkansas Laryngoscope, 1932, Mar Orbital abscess following submucous resection Female, aged 23 years, complained of constant dull headache of several years' duration There was a nasal obstruction and a septum resection was performed Severe reaction followed with orbital abscess Temperature rose to 103 degrees Fahrenheit, with edema, proptosis so extreme that loss of eye was feared Incision at inner angle resulted in pus drainage and eventual recovery with full vision

CASE 5 Dr Robert von der Heit, Chicago, Illinois, 1934, Sept Male aged 40 years Nasal origin, drainage from nose, antrum washings Incisions were made in both upper and lower lids Temperature at beginning was normal but increased to 102 degrees Duration was 3 weeks No incision was made in orbit, but drainage perforated connecting with antrum No mention of eye involvement was made

CASE 6 Dr E K Findlay, Chicago, Illinois, Illinois Charitable Eye & Ear Infirmary, 1934, Mar Patient had orbital abscess Drainage was established through incision in lids He was improving when he left the hospital

CASE 7 Dr A M Terson, Paris Arch d'opht, 1930, Mar, 181 Orbital phlegmon and its abortion Advises use of colloidal salts of silver and surgery when necessary

CASE 8 Dr M Halphen, Paris Arch d'opht., 1931, Oct, 727 Orbital phlegmon complicating ethmoiditis Exophthalmus was followed by bloody nasal discharge X-ray examination was positive for ethmoid involvement. Operation disclosed orbital nasal communication Recovery was rapid

CASE 9 Canuyt, Weill, and Horning Rev d'oto neuro-ophtalmol, 1930, June, 454 Suppurative frontal sinusitis opening into orbit A frontal sinus infection communicating with orbit, with proptosis and diplopia, necessitated surgical interference with drainage through an incision in the upper part of the orbit cavity and lid Recovery was slow, eye was deviated, and marked diplopia was present

CASE 10 Portmann, Teyssandier and Got, of Bordeaux Rev d'oto-neuro-ophtalmol, 1931, Aug, 355 Orbital abscess following frontal sinusitis Osteomyelitis of the orbital margin had resulted from extension from the frontal sinus Operation consisted in multiple incisions in the orbit and temple margins and removal of caries Convalescence was long and difficult, with high temperature Imperfect recovery The staphylococcus was isolated

[1] Arch Ophth., 1935 Oct., p 483.

CASE 1 Rebattu and Proby, of Lyons Lyons méd 1933 July 2 9 Fatal cerebral, following orbital, abscess A supra-orbital abscess was incised and the antrum drained A cerebral abscess developed causing death in 1 month

CASE 12 Prevot and Ourgaud. Rev d'oto neuro-ophtalmol 1934, Jan 35 Maxillary sinusitis with orbital phlegmon The antrum was washed after a tooth was extracted Immediately there followed pain in the orbit. Infection developed Drainage was established and patient finally recovered after repeated surgical interference This case is a warning against using pressure in irrigating cavities, it also shows the close relation of the orbit and cavities

CASE 3 J Kubik, Ehrlich's Clinic, Prague. Med Klin, 1932, Aug 5, 1037 Two cases of orbital abscess in meningitis following furuncles of scalp Each showed osteomyelitis of the antrum Recovery with vision saved

CASE 14 Paul Pomme, of Bordeaux Rev de laryngol 1930, Jan 15, 27 Orbital, following alveolar abscess An alveolar abscess extended through the antrum to the orbit Vision was lost

CASE 15 M Chase Read at sixty-eighth annual meeting, Belgian Society of Ophthalmology Arch d'Ophtal 1934, Dec 800 Three observations on phlegmon of orbit In the first case, a diphtheritic rhinitis, an orbital abscess was drained through lachrymal sac, with recovery In the second case, subacuous resection infection was drained through orbital incision with recovery In the third case, a wound of the eyelid, an orbital abscess developed with septicemia, a cavernous sinus infection which had a fatal termination

CASE 16 Rollet and Parthiot, of Lyons Arch d'Ophtal Mar 1931 176 Dentogenous maxillary sinusitis with orbital phlegmon An orbital abscess followed an antrum infection A Caldwell Luc operation was done, the opening being continued into the orbital cavity Patient recovered This case illustrates the possibility of drainage without external incision

CASE 17 P Dufong Arch d'Ophtal 1935, Mar 214 Orbital phlegmon Osteomyelitis of dental bulbs The first patient had necrosis of the maxilla and the second a venous thrombosis of the orbit, both infants recovered

CASE 18 B Strandbygaard, of Sonderborg, Denmark Ugesk f Læger 1936 Apr 15, 579 Two cases of orbital abscess The first a boy aged years, had an abscess of the orbit, which was opened through the antrum The second, a sister of 6 years, had a similar abscess, both drained several weeks Both recovered

CASE 19 L Gamet, Lyons Arch d'Ophtal 931 May 378 Thrombophlebitis of orbit Patient had a furuncle of the lower lip with extension to mouth, cavities, and left orbit High temperature, symptoms receded then came a relapse with general glandular and lung involvement At time report was made patient was living but condition was grave

CASE 20 P Moers, Tilleuont, Belgium Arch d'Ophtal 930, Sept 645. Reported at the Belgian Society of Ophthalmology Orbital phlegmon and diathermy Patient had a phlegmon of the orbit and face which was incised by diathermy knife The case illustrates the advantage of this method in which coagulation lessens the danger of spread of infection

CASE 21. Prof D Marzio, of Rome Rev oto-neuro-oftalmol 1930, Nov-Dec 544 Orbital complications of sinusitis Two cases are reported, both with perfect recovery by early operation on sinuses and drainage of the orbit.

CASE 22 Constantin and Bernas, of Bucharest Ann f mal de l'oreille, du larynx, 1937 July 693 Bilateral orbital abscess Three operations were performed first, on the mastoid second, on the lateral sinus; and third, both orbits were drained Convalescence was slow

CASE 23 Gaillard and Monnier-Kuhn, of Lyons Ann d'ocul 931, Sept 732 Bilateral orbital complications in exacerbation of sinusitis Patient had sinus infection of dental origin with orbital involvement and cavernous sinus thrombophlebitis Death occurred in 6 days Infection was carried to the cavernous sinus by the nasal and superficial veins Extensive operation was of no avail

CASE 24 Tauberova Karasekova (Brno) Fifth Czecho-Slovakian Congress of Ophthal Prague, 1930 Ann d'ocul 193 Nov 943 Two cases of orbital phlegmon In the first case, a metastatic infection of orbit in first week of enteric fever (Bacillus typhosus) was cured by vaccine and X ray without incision The second case, streptococcus infection of the orbit, was cured by incision and polyvalent vaccine.

CASE 25 G Luciano Boll. d'ocul 918, Jan, 78 Ethmoidal empyema of orbital origin Patient suffered pain in the orbit with occasional discharge of pus from the inner angle dust in eye caused sudden inflammation and exophthalmos At operation pus was found in the ethmoid and sphenoid It was concluded that infection was of ecto-orbital origin, as there had been no nasal symptoms

CASE 26 Monte F Meyer and Jerome C. Belsky, of New Orleans Arch Ophth 1935, Mar 445 Orbital abscess following foreign body in orbit Meningitis with recovery A piece of wood perforated the orbit, it was removed on the sixth day Orbit drained, but patient had marked meningitis, from which he recovered in about 2 months Also reports second case similar in that the spinal fluid was positive Patient finally recovered after decompression and serum was used

CLASSIFICATION OF CASES REPORTED

Visual acuity is so seldom mentioned in the case reports that it is impossible to classify from that standpoint however an imperfect classification may be of interest as determined in 33 cases

	Cases
Recovery saving globe or vision	15
Partial recovery, saving life but loss of globe	11
Fatal—loss of life	7

The etiological factors may be classified as follows

	Cases
Nasal sinus and dental	22
Infections of surrounding tissues	7
Metastases	3
Orbital origin	3

Discussion

Dr Raymond J Nuttings, Oakland. In opening the discussion I personally feel that Dr Orcutt is to be congratulated for bringing this very timely and too often neglected subject to our attention We all agree that early diagnosis with etiology is absolutely necessary, once this is established, active medical and surgical treatment is indicated immediately and, as we all know, by the time we see most of these cases, surgery is the one treatment par excellence in order to save not only vision but life itself

We have been very fortunate in our office, in the Cowell Memorial Hospital at Berkeley and in the County Hospital in Oakland, that the eye man has not opened the orbit in any of our patients with one exception in the last 10 years, and personally, I have not opened one in 15 years However, if our cases had been of the same type of infection as those treated by Dr Orcutt, I would not have hesitated to open directly into the orbit. In my private practice, orbital cellulitis has fortunately been secondary to paranasal sinus infection Of course the ear, nose, and throat man has had to share the responsibility and to co-operate with the oculist as each man must depend upon the other Of the cases that I have seen, with the exception of 2 from so called styes and another from a small furuncle on the forehead, all have been secondary to paranasal disease The interesting fact to me has been that the 3 cases mentioned all developed cavernous sinus thrombosis with a generalized septicemia In these cases the blood cultures were positive, 2 staphylococcus and 2 streptococcus All 3 died 2 in young girls, around 6 years of age, and 1 in a young girl about 20. Personally, I have not seen 1 death where there was an orbital cellulitis as result of paranasal sinus disease although they have been reported

I feel that we cannot overemphasize the importance of a complete and thorough rhinological examination when an orbital cellulitis is suspected, when not due to an external injury, and if at this time any positive or even suggestive signs and symptoms are found, immediate conservative or radical treatment is indicated at once depending of course upon the type of case

The signs, symptoms, and complications of orbital cellulitis, Dr. Orcutt has very well covered and the only suggestion that I might emphasize at this time is that, when there are no visual, ophthalmological, or field changes, conservative treatment can be attempted, but when definite eye findings are present, the more radical, surgical treatment is indicated and at once Many a patient has lost his vision and even his life because we have delayed surgical interference

In order to save time, money, and worry, when there are so many patients these days who are only too glad to start a law suit, it is important to have a blood culture made immediately on all these patients, and if there is any suspected intracranial involvement, a lumbar puncture as well is in order Such patients then cannot make the accusation that your treatment was the cause of septicemia or intracranial disease

Most of the cases we have seen have been in children When they were seen early, a good visual result was obtained But unfortunately, as mentioned before, patients wait too long before they call the doctor, naturally it is in these that we get our bad results No doubt this is one of the reasons why so many men get such a variety of results

Dr Orcutt is to be congratulated on his wonderful care in Case 3, especially with a positive blood culture Unfortunately, my 3 patients seen in private practice all died Autopsy revealed that all 3 had cavernous sinus thrombosis

No doubt, another factor in the cause of poor results in some of these cases in which the trouble is secondary to the accessory sinuses, is that conservative treatment has been prolonged, or that there has been poor co-operation between the oculist and the rhinologist Whether the nose man does an external ethmoidectomy or an intranasal operation, he must be thorough and in most cases he must open the orbit as well, so that drainage may be well established

Case 1 Boy "R," aged 12 years went swimming April 14 1933 April 16, he had stuffy left nostril and pain in left eye April 17 he was seen by his physician who suspected sinusitis and gave him ephedrine nose drops and hot packs April 18, he had a swollen eye, pain, exophthalmos, and poor vision April 19, he was seen by me at his home Diagnosis orbital cellulitis and optic neuritis. Vision in left eye, was questionable He was sent to the hospital immediately and blood culture was returned negative He was seen by Dr McClure, who made diagnosis of acute purulent left pansinusitis X-ray examination was positive. Operation was performed by Dr McClure, intranasal opening of ethmoid radical external ethmoidectomy including opening into orbital cavity A large amount of free pus was found in the orbital cavity, the ethmoids and sphenoids were filled with pus under pressure. A rubber draining tube was introduced Dr Hans Barkan was called into consultation May 10, nervehead was getting pale secondary atrophy had occurred, eye was blind but had good movement Bad visual result was obtained as operation was necessary before visual changes had taken place

Case 2 Male J, aged 54 years, complained of swelling of right eye. He was seen on August 6, 1935 History 4 weeks previous the right eye became very tender and painful especially in the forehead region He saw a doctor at this time to have his glasses changed No drooping of right upper lid was noticed until observation of picture 7 years ago. Examination disclosed vision 20/20-4 in the right eye and 20/20 plus in the left Upper lid was swollen and edematous—exophthalmos Eyeball was pushed down and out Eye grounds were entirely normal Diplopia was present but worse up and down He was referred immediately to Drs. McClure and Keeler who made a diagnosis of chronic right frontal and ethmoiditis at that time Conservative treatment of the nose was started, and on August 7 a large polyp was removed from the middle meatus, followed by a profuse continuous drainage Both antrums were opened On August 8 radical Killian procedure was advised On September 3, the usual Killian incision was made and the anterior wall of the frontal sinus was found to be definitely infected Thus

was removed and the cavity was found to be filled with pus under pressure and to contain considerable granular tissue. The dura was exposed and was found to be covered with granular tissue over an area of about 3 by 4 centimeters, the whole posterior wall of the frontal sinus having been destroyed. The anterior wall and the floor were removed entirely and the granulation tissue curetted away as far as possible. The ethmoids were then opened anteriorly and large amount of foul pus was again found under pressure in the posterior ethmoidal region. The ethmoidal labyrinth was completely exenterated and the middle turbinate was removed. Satisfactory drainage from the frontal to the nasal cavity was obtained, except that there was such an extensive necrosis that it was not possible to retain large canal. The whole medial wall of the orbit was removed, and at the close large amount of foul smelling pus was found. The wound was packed to the nose, with vaseline gauze. The anterior incision was closed in the usual manner, and wet dressing was applied.

Diagnosis: Chronic right frontal sinusitis with extensive abscess. Chronic right maxillary sinusitis and ethmoiditis. Orbital cellulitis and phlegmon.

Eye examined October 16 showed vision 20/ 6 in each eye. Eye grounds were entirely normal, there was no exophthalmos, and no diplopia. Visual fields were normal.

CANCER OF THE LARYNX[1]

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IN my discussion only the intrinsic cancers of the larynx were considered. A brief review of the history of cancer of the larynx was given, with a comparison of the results obtained in the treatment of cancer in other parts of the body. The question of the increase of cancer in general and of laryngeal cancer in particular was discussed together with the possible influence of smoking. Alteration of the voice as an early symptom of intrinsic cancer was pointed out, and the disregard of this symptom by both the laity and physician was deplored.

The difficulties of diagnosis in the early cases were stressed, together with the value of careful clinical observation, but the final proof that a growth is malignant and the degree of malignancy must be made through the aid of the microscope.

The dangers of stimulating the growth and producing metastasis by removing portions of the tumor has not proved to be as grave as was formerly believed. Attention is called to mistakes made in diagnosis from poorly collected specimens. The pathologist's report should always be backed up by the clinical findings.

The curability of early cancer of the larynx, when the growth is confined to one vocal cord, varies from 75 per cent to 84 per cent. Unfortunately less than 10 per cent of the cases present themselves for examination when such results are possible.

The 3 methods of treatment are: (1) removal of the growth through laryngofissure; (2) complete removal of the larynx; (3) radiotherapy. The choice of treatment depends upon the individual case, the location and extent of the lesion, and the degree of malignancy.

The mortality following the operative procedures, owing to pre-operative care and refinements of technique, has been reduced from 50 per cent to 3 per cent. The importance of the after-care, with consideration of the complications that may arise, are taken up. The value of intravenous injection of neosalvarsan in the treatment of spirochetal infections of the wound and lungs is reported. Radiotherapy of cancer of the larynx has not given results comparable to surgical removal, and laryngologists are loath to risk their early cases to this form of treatment until more time has elapsed and radiotherapy has proved itself. Recent reports of this form of treatment offer more encouragement.

[1] Abstract of paper presented before the Clinical Congress of the American College of Surgeons, San Francisco, October 28-November 2, 1928.

A RÉSUMÉ OF ONE HUNDRED TRANSANTRO-ETHMOSPHENOID OPERATIONS[1]

CHARLES EDWARD FUTCH, M D , F.A C.S , Los Angeles, California

THE problem of surgical relief of sinus disease is a challenge to each of us as rhinologists The contributions in this field in the last decade by Lynch, Sewall, Turnbull, and Ferris Smith are monumental, but as sinuologists we must surpass our previous efforts if the prejudice of the profession and the layman is to be amended

TECHNIQUE

I appreciate this opportunity to acknowledge my gratitude to Dr Frederick M Turnbull, who patiently instructed me in the technique as published by him In the following series of cases, this technique has been my choice which, in one operation, accomplishes adequate approach, removal of the diseased tissue, and aeration It is generally recognized that the ethmoids are the crux of success in this work. These cells are present at birth and by their anatomical nature and poor drainage are the most frequently and chronically infected In some cases a complete exenteration of the ethmoid cells is impossible by any technique because of postorbital or pterygoid extension As stated by Frederick Law "Unless the surgeon has knowledge of the anatomical structure and measurements to guide him into this separate ethmoidal cell, he is liable to leave this diseased cell, and the results of operation will be unsatisfactory "

Mosher states that the incidence of ethmoid cells outside the true ethmoid capsule is only 5 per cent. This 5 per cent of the diseased cells means a 5 per cent failure if they are not removed, and this percentage, plus that resulting from surgical imperfection, is too high to result in a reasonable satisfaction either to the patient or to the surgeon

In 98 per cent of these cases surgical antral disease was diagnosed Frontal disease was present in only 2 per cent In the choice of the transantrum technique, relief of the most frequent combination of pathological conditions was accomplished, and drainage of the frontal sinuses was improved in 1 operation without surgically entering the frontal sinuses

PRE-OPERATIVE STUDY

A definite routine of study leading up to diagnosis was used in each of these cases A history was taken and primary study made upon the first visit If sinus disease was definite or suspected, X-ray films were ordered As a rule, no sinus irrigations were indulged in before X-ray study, but if irrigations had been done, 3 to 4 days were allowed to elapse before the X-ray pictures were taken

Too much stress cannot be placed upon the importance of X-ray study The films should be taken by a roentgenologist who has made a specialty of such work The stereoscope which is fitted with the Pancro mirrors as have been developed by Turnbull, has proved to be of great assistance in my later cases in the localization of disease

Upon subsequent visits nasopharyngoscopy was done repeatedly, with particular attention to the sinus ostia Irrigations of the antra and sphenoids were likewise done, isotonic sterile saline at 105 degrees F being used The antrum irrigations were all done through the middle meatus, approximately 85 per cent through the natural ostia, a Fletcher Pierce sterling silver cannula being used The occasional case in which the natural ostium was not found was irrigated with the Larges semi-sharp antrum cannula The sterling silver Brown sphenoid cannula was used in the sphenoid technique The flexibility of this cannula made it possible to irrigate around most septal deviations and hypertrophied membranes

The clinical findings, observations of return fluid upon irrigation, and X-ray study determined the type and degree of pathology in each case

INDICATIONS

In this series of cases, diagnosis of sinus infection plus the constitutional picture and history were used as the basis for surgical indication A patient with a high degree of sinus disease but with no marked constitutional reaction or disability will not appreciate surgical intervention although it may be theoretically indicated, on the contrary, a patient with only a minor degree of sinus trouble but with an almost complete arthritic, cardiac, or other disability may fail to improve with all efforts except by exenteration of the sinus disease Regardless of the pathological condition present, except in definite polypoid or cystic degeneration, irrigations and the usual conservative therapeutic measures were carried out, and occasionally in those cases with purulent involve-

[1]Presented before the Clinical Congress of the American College of Surgeons, San Francisco October 28–November 1, 1935

ment and apparent metaplasia, such improvement was noted clinically and constitutionally that only conservative surgery if any was concluded.

In the classification of indications for radical surgery Skillern names the "absolute and relative" and it may be of interest to note that only two of this series fell under the absolute (immediate) classification. In both of these cases the frontal sinus was trephined immediately The other sinuses were treated conservatively at the time and were operated upon at a later date with the transantrum technique.

We may deduce without hesitancy that sinus surgery should be, and is, based upon the same principles as other septic surgery In the more acute phases, local drainage, aeration, and constitutional treatment is sufficient, but in the chronic phases of the disease nothing less than the complete removal of the septic tissue is of avail Quoting Proetz "There are only two surgical objectives to be considered the first is ventilation and drainage and the other is complete eventeration.

PRE-OPERATIVE CARE

In all cases of this series a complete medical examination was insisted upon before operation. In the last 40 cases, an electrocardiogram was required, as in several of the earlier cases post operative cardiac complications developed. In those cases in which the patient showed any kidney involvement other than albuminuria, a kidney function test (6 cases) was required

Patients in which the membranes were markedly purulent were given a course of sinus irrigations in an effort to reduce the inflammation and infection before the operation. In about 5 per cent of these patients, antrum windows were made and irrigations were continued until the inflammation was reduced as observed with the nasopharyngoscope.

ANESTHESIA

The anesthesia in the last 64 cases was greatly improved over that in the first cases by the use of avertin (tribromethanol) It has been possible by the use of this drug as a basal anesthesia for the patient to approach the operation with the minimum apprehension and for the surgeon to proceed under less pressure. This anesthesia, as used in the later cases began when the patient entered the hospital, at which time 1½ grains of pentobarbital was given and repeated at 8 p.m. and at 6 a.m before operation thus assuring the patient a restful night and resistance to cocaine poisoning Twenty minutes before operation, the nose was packed with thin pledgets moistened with equal parts of 10 per cent cocaine and 1:1000 adrenalin, applied to each of the meatuses. Immediately following this local application the avertin was administered by an anesthetist skilled in its use and the patient was taken immediately to the operating room where the block injection, according to the Turnbull technique, completed the anesthesia. It has been found unnecessary to inject the palatine nerves since avertin has been used. The operation was begun as soon as the injection was completed

The chief contra-indication to avertin is organic disease of the liver therefore in very toxic cases, the liver function test is indicated. Bilateral kidney lesions and acidosis are also contra-indications to the use of avertin. Alpha lobelin is an active antithesis and should be kept in readiness In the total series of cases there were no anesthetic complications or unpleasant sequelæ.

OPERATION

This paper does not deal with operative technique, but one principle should be emphasized. the removal of the nasal wall of the ethmoid capsule with the superior turbinate. I am aware of the discussed danger of opening the perineural sheaths of the olfactory nerves and the consequent possibility of meningitis. This misfortune has not been encountered, and I feel that the subsequent benefit of this procedure more than justifies the risk. This method likewise has been criticized because of the destruction of the lateral branches of the olfactory nerve, but as the septal distribution is anatomically greater and as a large percentage of these patients complain of an impaired sense of smell before operation, I cannot but again feel justified. In this series of cases, there has been no case in which the partial loss of smell has been permanently a major complaint, and several have stated an improved olfactory sense.

COMPLICATIONS

At the time of operation, hemorrhage was a complication which gave much less trouble than was expected, and no uncontrollable hemorrhage was encountered during actual surgical procedure In the order of importance, bleeding occurred at operation from the following vessels. the anterior ethmoidal artery the pterygoid plexus, the sphenopalatine artery and the posterior ethmoidal artery Hemorrhage from the ethmoidal arteries was controlled by adrenalin sponges in situ. In 7 per cent some bleeding persisted when the operation was completed and in these cases a one-fourth inch phenolated vaseline packing was left over the bleeding point and removed through

the nose during the next 24 hours In 4 per cent, the sphenopalatine artery was tied off at operation by use of the Sewall sphenoid ligature instruments This procedure was not difficult with these instruments when the mucous membrane, with the periosteum, was dissected down from the anterior face of the sphenoid sinus I feel that the security of this practice is well worth the short time involved

Postoperative hemorrhage was more troublesome In 1 case hemorrhage from the sphenopalatine artery was uncontrolled by packing, and, due to the free bleeding, ligature was impossible in my hands The external carotid artery was tied off with immediate control A similar hemorrhage and control occurred in 1 case 8 days after operation In 4 cases less profuse hemorrhage occurred between 4 and 14 days after operation, all of which were controlled with packing I no longer consider the possibility of hemorrhage as formidable as in my earlier cases

In 2 cases there was a continuous drainage of clear fluid for 4 or 5 days after operation, both from the left side of the nose No unusual headache or temperature was present. It was my opinion that this drainage was spinal fluid and that the dura undoubtedly had been injured at operation Fortunately, the flow of fluid protected against infection in these cases, but such good fortune can hardly be routinely expected In 1 case, during anterior ethmoid exenteration, the dura was exposed for an area 4 by 4 millimeters, probably due to surgical fracture There was, fortunately, an uneventful recovery in this case.

Halle states that he has never seen an operative laceration of the dura. He has seen dehiscences exposing the dura, but he believes that such exposure is no more dangerous than similar exposure of dura in mastoidectomies

Light shock was encountered in 3 operations, in each one during the ethmoid surgery The operation was in each case continued after lowering the head and administering alpha-lobelin Profound secondary shock was encountered in 2 cases in which bilateral operation was done This experience did not always accompany the bilateral procedure, but it is questionable if such shock would have occurred had the operation been divided In 4 cases the primary incision had to be freshened secondarily and sutured 2 to 3 weeks after operation, due to persistent fistula

MORTALITY

At this time there has been no primary or secondary death in this series One patient in profound shock was in a serious condition for 36 hours and showed a temperature peak of 108 2 degrees F following a carefully matched transfusion A subsequent uneventful recovery followed this stormy period Halle states that in 1000 operations on the ethmoid process, he has not seen more than 1 fatality from meningitis

POSTOPERATIVE CARE

The briefest period of postoperative care was 6 weeks and the longest period of care was 4 months The average of this period has been 8 weeks The longest hospitalization was 29 days and the shortest period, 8 days The average hospitalization was 13 days I have not felt it advisable to discharge these patients from the hospital in 2 or 3 days, as some cases have been reported It has been my opinion that the neuralgias and the danger of a neglected hemorrhage, as well as the need of complete rest, make longer hospitalization advisable

A 10 per cent solution of dextrose, 500 to 1000 cubic centimeters, was slowly administered to each case after operation While in the hospital, the patients were treated every day with applications of 1 per cent ephedrine and 10 per cent cocaine (equal parts) followed with argyrol packs Beginning the fourth day, a gentle nasal lavage was given, with normal saline solution at 105 degrees

The average number of office visits for postoperative care was 3 visits each week for 2 weeks, then a gradual decrease in number until the patient was discharged In justice to the operation and to the patient, we refused to state a definite period of postoperative care, as the time varied in the individual case When discharged from regular office visits, each patient was advised to report immediately for treatment in the event of an acute rhinitis The average number of colds after operation was much lower and the duration much shorter

PATHOLOGY

The pathological process in each of these cases had reached a stage that resisted conservative surgical efforts and treatment. In the majority of cases the tissues seen at operation bore out the pre-operative diagnosis, in approximately 10 cases, the condition was worse than anticipated In most of these 10 cases, however, the condition was of many years' standing and a high degree of osteosclerosis masked the soft tissue pathology, particularly that of the antra

RESULTS IN SPECIFIC COMPLAINTS

One case of tic douloureux of 6 years' duration was relieved and has had no recurrence since

operation 2 years ago. Clinically the nose appeared clear but transillumination and X-rays showed an old involvement. Irrigations showed foul granular pus repeatedly from the right antrum. The patient was carefully instructed before operation that our efforts were aimed at relieving her of her sinus disease, but we could not assure her of relief of the tic douloureux.

Six patients had asthma of various degrees. The 2 patients most severely affected were entirely relieved for 2 years then 1 had a severe recurrence. Examination in this case showed some cupping and retention in the left sphenoid by the not unusual secondary cicatrix. The removal of this obstruction to drainage has given the patient much relief although not so complete as was experienced for the first 2 years. The 4 other patients have shown some degree of improvement.

Four patients, definitely allergic, were studied and treated by the allergist. The superimposed infection of the sinus membranes persisted and surgery was concluded before the patients enjoyed a degree of nasal comfort. It has been my experience that a patient who has suffered a protracted exogenous allergy not infrequently suffers from a superimposed deep seated infectious sinusitis which does not clear up with desensitization and as is well known, those patients may develop an endogenous allergy to this infection. The 4 cases mentioned undoubtedly fell into this classification.

BACTERIOLOGY

In this series of cases, no original bacteriological studies were made. The rationale of surgical procedure has, however been based upon that work done by Kistner Rosenow and others. Upon tissues removed from hyperplastic sinuses and sent to Dr Rosenow at Rochester by Dr Kistner a brief of the report was as follows "Unmistakable organisms were found in all tissues and the bacteria were by far the most numerous in the deep layers next to the periosteum and least numerous on epithelial surfaces." Certainly the surface treatment of such tissue could be expected to accomplish little more than could be expected from external application to chronic tonsillitis.

We have had some success with the Krueger autogenous vaccine, but only in cases in which the pathological condition was not degenerative. At present I have more confidence in surgery for cases in which there is a marked pathological condition and symptoms. Vaccines, in a few cases before and after surgery have been valuable adjuncts.

CONCLUSIONS

Thanks to the efforts of the pioneers in this work, to some of whom I have the honor to present this effort, our status in sinus surgery is far removed from that stated by Robert Lynch only a decade ago "One treads with fear and trembling when thinking of the care of a condition so distressing and fraught with so much misgiving as a chronic frontal sinusitis, or even more so the chronic pan sinusitis." Rather should we proceed in confidence with that technique which serves us best to relieve our patients of a pathological process which, until recent years, was held intractable.

SUMMARY

In complete sinus surgery the transantrum technique permits the removal of pathological processes from the antrum, ethmoids, and sphenoids at one operation. The high percentage of antral disease associated with ethmoid disease makes this approach preferable to one which neglects or defers the antrum disease until a second operation.

In each of a series of 100 cases in which the transantrum technique was used, the condition was considered surgical only after clinical and X-ray study to determine the extent and gravity of the pathological process. Surgery was carried out only when the severity and persistence of the chief complaint justified the measure.

Basal anesthesia with avertin was a valuable adjunct to the usual cocaine and block anesthesia. No complications were noted in our series.

At operation, the nasal wall of the ethmoid capsule with the superior turbinate was removed. There were no complications and no pronounced loss of the olfactory sense.

Hemorrhage was countered by packing or suture at operation, and by packing after operation. The external carotid artery was ligated in 2 cases.

In 2 patients drainage of spinal fluid was present for 4 days. No resultant symptoms were noted. The dura was exposed in 1 case with no complications.

Shock in variable degrees occurred in about 10 cases, all being bilateral cases. Unilateral operation with the second performed at an interval of 1 week is advisable rather than bilateral operation at 1 sitting.

Pulmonary embolus occurred in 1 case.

The average hospitalization was 15 days the average postoperative care extended through 2 months.

In 1 case of tic douloureux the patient has been relieved since operation 2 years ago.

In 6 cases of asthma patients have all shown definite improvement, 1 has been entirely relieved since operation 2 years ago

Four patients desensitized to their primary allergy were not relieved until the secondarily infected membranes were removed

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UNIQUE SYMPTOMS AND EFFECTS OF SPHENOIDAL DISORDERS[1]

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THE sphenoid sinus, situated as it is in the center of the skull, may be in relationship with the three cranial fossæ and half of the cranial nerves and important blood vessels. It often occupies one third of the middle fossa in the lateral diameter. When diseased, it gives symptoms which are most unexpected and bizarre. In many cases, very little emphasis is placed on the clinical picture presented by patients suffering with sphenoiditis and too little time is devoted to the otolaryngological study. Patients with sphenoiditis show numerous, perplexing, and variable signs and symptoms and since they are often in the realm of neurology are referred to the neurologist for diagnosis. He in many instances, overlooks the possibility of sphenoiditis because of his lack of familiarity with the symptomatology of this disease.

Infection of the sphenoid sinus alone is probably rare but frequently the involvement of the posterior ethmoids clears up, due to their better drainage, thus leaving the sphenoids alone the sole center of disease. Of all the sinus suppurations, the sphenoid is the most dangerous because of its being surrounded by the meninges, the cavernous sinus and its contents, the carotid artery, the hypophysis, the optic nerve and chiasm. No doubt some sphenoids with a low grade infection have escaped detection for years, having been considered merely a chronic catarrhal condition until the sudden appearance of a severe ocular disturbance or another complication has invited immediate attention. In fact Vail reported the examination of 75 pairs of sphenoid sinuses removed routinely at autopsy at the Cincinnati General Hospital. All the cases were on services other than nose and throat. Five patients showed gross infection of one or both sphenoid sinuses. After going over the histories, there was nothing to suggest that there had been any suspicion of sphenoid sinus infection. Apparently the infection in the sinus was not in any way a factor in the death of the patient, but at any rate in 5 of 5 cases, there existed an obvious chronic suppurative sphenoiditis not recognized during life. McKibben, at the medical department of the University of Southern California, found the same percentage of non-detected sphenoid suppuration in the dissection room.

Since every rhinologist today is familiar with the anatomy it is unnecessary to say anything more than to call attention to the enormous variation in size and the consequent variation in relationship which occur with this sinus. The sinuses are frequently asymmetrical, one sinus frequently occupying much more of the space than the other at times the involvement of one sinus being so great as to involve both optic or both vidian nerves. There are always two ostia but the dividing partition may be considered as radiating to any degree like the spokes of a wheel. Dehiscences in the bony wall are often present thus placing the sinus mucosa in direct contact with the optic nerve. In several postmortem examinations, the vidian nerve lay bare in the sphenoid cavity without any bony covering and therefore subject to immediate inflammation when the sphenoid was involved. It will be recalled that the vidian nerve runs on the floor of the sphenoid sinus and any excessive pneumatization will hollow out the pterygoid plate lateral to the nerve in such a way that a deep recess may be formed. Any infection getting into such a sinus usually gravitates toward this recess and readily forms a focus of infection which is very resistant to any form of treatment.

The vidian nerve and its many ramifications are responsible for many of the symptoms which confound the clinician. The external wall is frequently the thinnest, being often the thickness of a cigarette paper with dehiscences occurring in it, especially if the sinus is large. This wall helps to form a portion of the middle cranial fossa and is in direct communication with the cavernous sinus, the outer or external wall of which contains the internal carotid artery and the oculomotor, trochlear and the ophthalmic and maxillary divisions of the trigeminus and abducent nerves.

The optic nerve crosses the upper and lateral angle of the sphenoidal sinus. Hulson states that in cadavers which he studied, the thickness of the bony plate between the optic foramen and the contained optic nerve and the cavity of the sphenoidal sinus varied from total absence to 2 millimeters. In many cases the thin wall of the sinus was found pushed into mound-like relief by the nerve, so that in a sense the nerve passed through the sphenoidal sinus and was separated from the cavity merely by this bone and, when osseous deficiency existed, only by the mucous membrane. He says further that the optic

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commissure is always in the roof of the sphenoidal sinus As the ostium of the sphenoidal sinus is high up from the floor, usually about 1 centimeter, drainage often is poor, and pus may rise as high as the optic foramen before it can escape into the nasal cavity or can be confined under pressure in case the natural drainage is obliterated

The (5) anterior wall interests us most from the surgical standpoint as it is the only one accessible to approach Within the mucous membrane covering the anterior wall, we have the pharyngo-palatine artery This fairly large artery when torn or cut, causes frightful hemorrhages Sphenoidal infection may take place in children, the sinus is fully formed by the fourth year Myerson has reported a death in a child, 5 years old, from meningitis in which the sphenoid sinus showed pus

Sphenoid sinusitis may be classified as acute and chronic We will pass over the acute form by merely mentioning that the symptoms are similar to those of the chronic form, except that the attack is sudden the headache, neuralgic pains, and tightness in the head are most intense, and the vertigo is pronounced The optic neuritis may result in transitory blindness, and the field of vision and color acuity may be so affected as to produce a temporary color blindness and tubular vision The various symptoms associated with sphenoiditis are subjective, objective, general and ocular manifestations which vary from headaches to the peculiar syndromes, some of which are seemingly unattached to the sphenoid The symptoms are dependent upon the type of sphenoid, the abnormal anatomical situations, and the degree of extensions of the pathological process Of the different types, the hyperplastic is the most variable The opinion is prevalent among otolaryngologists that many of these patients come to them with conditions previously diagnosed as neurasthenic.

Among the subjective symptoms (7) is headache from irritation of the vidian nerve and sphenopalatine ganglion, which pains are typically sensory along the distribution of the fifth nerve They are sharp and severe (3), beginning along the side of the nose, passing into the eye, temple, ear, mastoid, back of head, shoulder, and down the arms The headache situated in the occipital region radiates in fan-shaped formation upward toward the vertex This pain was formerly considered as a reflex through the vertical nerves It is very different in character from the pain in the trigeminal region and is more likely to be of vasomotor origin due to a spasm of the occipital artery Investigation has revealed the anatomical knowledge of the sympathetic nerve fibers associated with the carotid artery and sheath pressure exerted over this region produces or increases sphenoidal pains when this sinus is affected Many other reflex pains associated sufficiently often add to the complex symptoms Ridpath (4) mentions two of these a reflex pain felt over the canine tooth on the side affected, and pain of a burning or continuous character at the junction of the soft palate with the anterior pillar of the faucial tonsil A third is a dull, sickening pain of continuous character felt over the pyriform crest Pain in the ear is also common and may be very severe simulating the pain of acute otitis media

I would like to report a case in which the ear symptoms predominate

Case 1 Mrs L , aged 33 years when first seen complained of headache deafness, pain in both ears, loss of memory and insomnia, temperature was from ½ to 2 degrees above normal almost daily Onset of present illness began 10 months previously with pain in left ear which broke and discharged for a few days This ear cleared up but several months later pain developed in the right ear There had never been any previous head symptoms except an influenza 3 years ago Since that time the patient had had rather frequent colds and postnasal discharge About 1 year ago, pain occurred in both ears, sharp and severe, and the hearing became worse and worse Because of the daily temperature, her physician suspected pulmonary tuberculosis and the patient was put to bed for several months Ears did not discharge again but deafness increased to the degree that she could barely hear ordinary conversation

Headache Throbbing pain in vertex was made worse when she stopped over The pain was referred to the ears and seemed deep seated She had consulted several physicians and head specialists with no relief, and with varied diagnoses Ear inflations did not improve deafness Because of the long duration of symptoms and the fact that the patient lived out of town, she was admitted to the Good Samaritan Hospital for diagnosis The following pertinent facts were found during her sojourn in the hospital daily temperature 99 to 100 5 degrees, leucocytosis from 10 to 11 thousand, blood and spinal Wassermann negative, as were examination of chest, urine, and stools and neurological examination of cranial nerves Roentgenographic study of the skull, sinuses, and mastoids showed nothing suggesting pathological change in the skull proper The sphenoid was about half pneumatized in the anterior portion, the sella was normal in appearance, nothing suggestive was seen in the vault The mastoids were normal throughout Roentgenograms of the sinuses showed normal appearing symmetrical frontals, also normal appearing ethmoids and left antrum The right antrum showed definite thickening and roughening of the wall There was a definite fuzziness in both views made of the sphenoid in the Granger line X ray conclusion was bilateral sphenoid pathology

Otolaryngological study Weber test revealed bone conduction to right and less than normal Hearing for conversation, one-third of normal in right and one-fifth in left. Loss of hearing for both high and low tones was in about the same percentage. Both membranes were thick and

definitely retracted There were no perforations Tenderness was noted over both mastoids Other cranial nerves were found normal Cerebellar tests gave normal reaction The tonsils had been well removed, but there was a small amount of mucopurulent discharge on the postpharyngeal wall Both middle turbinates hugged close to the septum. Probing and washing the sphenoid always caused severe pain in the ears, the same pain that the patient complained of continuously Both sphenoids were opened under local anesthesia after removal of the posterior half of both middle turbinates The membrane was found to be thick and polypoid and purulent material was removed

Convalescence was satisfactory in every way The sphenoids were washed until the discharge disappeared Improvement in hearing was almost immediate and the patient was delighted that she could hear the radio in an adjoining room as well as sounds which she could not hear before Within 2 months hearing was improved 100 per cent in both ears without other treatment The temperature became normal as did the leucocyte count, and all pain disappeared

This case is interesting as the patient had been in bed for several months because of fever She had been advised to have a mastoidectomy because of pain She had such severe pain in the ears that she required narcotics daily for several months Her symptoms were all referable to some other place than the nose except for a slight postnasal discharge and yet the symptoms all disappeared when the sphenoids were opened and drained.

Frequently conditions of the eye or in vision are the causative factors in referring patients to a rhinologist Much confusion has arisen in the past as to what causes of choked disc are the result of mechanical factors and what ones are the result of swelling of the nerve head due to toxic sources It is admitted that the most frequent cause of papilledema is an intracranial lesion However the case reports of competent observers would seem to bear out the fact that marked papilledema may be produced by factors other than a serious intracranial lesion, for instance by a purulent inflammation of the sphenoidal sinus While I am opposed to undue haste in deciding to open a sphenoidal sinus and in the performance of unnecessary operations, yet I believe we are not justified in following a conservative course when the diagnosis seems fairly conclusively determined as a result of a cooperative study by the ophthalmologist rhinologist, and roentgenologist. The possible consequences of delay are too serious to justify temporizing, particularly when the operation on the sphenoid is a relatively safe procedure from an operative standpoint So many cases of optic involvement with associated sphenoidal infection have been reported that we will omit reports of cases of this sort A most interesting case developed in an X ray technician who has been under the care of my associate, Dr Colby Hall

CASE 2 A S 22 year old girl, in June, 1934, noticed a blurring of vision She noted that she could read well with either eye but binocular reading was impossible Neurological examination revealed no disease Repeated fundus examinations revealed normal nerve heads Neurological examination, including spinal fluid, revealed no abnormality Patient had a definite defect in convergence and accommodation, the large E on the eye chart being blurred or double at 20 feet repeatedly One day she reported with an intense dull pain behind the right eye The region of the right sphenoid antrum was cannulated to a depth of 7 5 centimeters and warm saline irrigated through the cannula This was followed by relief of pain No discharge was recovered The patient called the next day and said that her vision had been normal for nearly 8 hours This process was repeated many times with the identical result Blockage of the antrum was followed by no relief Irrigation of the maxillary sinus gave no relief and neither did treatment of the left sphenoid The relief in vision was almost immediate before the cannula was removed X-ray examination demonstrated that the cannula was not in the sphenoid sinus but flush against the face of the sphenoid A few months ago the sphenoid was opened A slightly thickened membrane was found but no discolouration Irrigations of the sinus since then have given the same results Occasionally the vision is restored to normal for 10 to 2 hours

In this case there is no question of optic nerve involvement, but rather the muscles of accommodation undoubtedly we are dealing with a very thin external wall of the right sphenoid possibly with a dehiscence.

Time will not permit the report of more cases, but in conclusion I would like to emphasize the importance of the investigation of peculiar syndromes in the head which are seemingly unattached to the sphenoid The unfortunate lack of knowledge not only from the standpoint of the medical man but also from that of the neurologist and rhinologist, leaves many cases unsolved The more this sinus with its symptoms is studied, the more one will appreciate the likelihood of its being a focus of infection.

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MANAGEMENT OF COMPLICATIONS IN THE OPERATIONS FOR CATARACT AND GLAUCOMA[1]

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SOME form of conjunctival flap, I believe, is definitely effective in the management of complications in operations for cataract and glaucoma. The principal service of the flap is not to hold back the vitreous that threatens to escape, but to prevent an eversion of the corneal flap, and to contribute to a sure, rapid, smooth, and uncomplicated process of healing

The conjunctival flap can be more accurately fashioned before the incision is made, and one or more sutures inserted before the delivery of the lens will almost invariably maintain satisfactory relations of the lips of the incision The most ideal results have been achieved by me when an uncut conjunctival bridge has been used It is somewhat more difficult in execution, but it makes for safety and prompt recovery

PROLAPSE OF VITREOUS

Vitreous loss alone in moderate amount does not preclude a good result, but if possible the loss should be prevented or reduced to the minimum If the vitreous is known to be definitely liquefied and the choroid seriously degenerated, operation is contra-indicated If the vitreous is normal, I proceed promptly with an intracapsular removal I use the flat spatula of Smith which is passed down into the vitreous and serves as an inclined plane upon which the intact lens can be made to glide upward and outward when external pressure is judiciously and gently applied This procedure when mastered is practically always successful in saving both the lens and the vitreous It is especially important that the capsule should not be ruptured in such cases, thus leaving retained capsule and cortex to blend with traumatized vitreous, which might lead to cataract and delay recovery Of course, it is always essential to make a correct incision If in doubt, a shorter incision should be made with the knife and if necessary enlarged with scissors

Anesthesia—local and general In practically all adults, I depend on local anesthesia, according to the accepted modes of application, although I have found intravenous injections of barbituric acid salts wonderfully satisfactory, except in patients with idiosyncrasies to these agents When the electrocautery is to be used, as in the removal of malignant neoplasms, the barbiturates are especially indicated, as inflammable anesthetics, like ether and ethylene, could not be used The skillful administration of chloroform has many advantages and I have encountered no accidents in its employment When necessary to supplement the bromides or barbiturates by mouth, I have found pantopon or some other morphine derivative given hypodermically to be safe and efficient

Expulsive hemorrhage This dire disaster cannot be foretold It is not dependent upon increased intra-ocular pressure and not necessarily associated with arterial hypertension or vitreous loss It seems to depend upon vascular degeneration of the choroid and may occur during, or at any time within a few days after, the operation If large vessels rupture, the case is hopeless If smaller vessels rupture, the hemorrhage may be arrested by elevation of the head, gentle pressure upon the closed lids, and a few whiffs of chloroform pending the action of morphine or pantopon administered hypodermically I have seen these measures succeed Many complications may be avoided by promptly closing the lids the moment the essential steps of the operation have been effected

Infection—exogenous and endogenous With thorough precautions, exogenous infections can almost be eliminated, but endogenous infections occasionally may occur in vulnerable patients In these latter patients, injections of various proteins may be quite effective From an operative standpoint, the uncut conjunctival bridge and reduced trauma will be the chief factors of safety

Postoperative glaucoma The measures of supreme importance in preventing and in controlling this complication are keeping the inflammatory exudates away from the filtration angle, quick union to prevent epithelial proliferation within the anterior chamber, avoidance of after cataract with the consequent needlings, and the judicious regulation of mydriatics and miotics with careful systemic attention Needling involves quite as much hazard as the original extraction because this means excitation within the closed eyeball without the safety of drainage

Epithelial ingrowth The greatest safeguard against this complication would be an adequate conjunctival bridge insuring a speedy closure of the incision

Retinal detachment The prevention of retinal

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detachment is in the elimination of excessive vitreous loss and of chronic uveitis with a softening of the globe. The cure, if possible, depends on one of the modern surgical procedures, combined with rest and judicious local and systemic management.

Sympathetic ophthalmia. This complication, so far I have encountered once after careful cataract extraction and once following a smooth Elliot trephine operation, but it has occurred many times in better hands than mine. Our great master in ophthalmic surgery Herman Knapp of New York, has reported an average of 1 case of sympathetic ophthalmia in every 750 of his cataract operations The unrivaled pioneer ophthalmic surgeon, Albrecht von Graefe, encountered this disaster so often in his modified linear extraction that this particular method was largely abandoned.

The prevention would be in avoiding those factors that favor a prolonged iridocyclitis with a non-suppurative weeping eye. In suspicious cases, the measures advocated years ago by our honored confrère, Harold Gifford, of Omaha, still stand pre-eminent.

Iridectomy What to do with the iris has always been an important question. The dictum enunciated long ago by that princely surgeon, Henry Power of St. Bartholomew's Hospital, London, embraces a golden truth "When no complications are threatened, a round pupil is best, but when difficulties or dangers are encountered, perform an iridectomy"

A more extended consideration of the use of the undivided conjunctival bridge in operations for cataract and glaucoma This phase of the subject relates to the employment of the uncut conjunctival bridge, which is an ancient and well established objective. The literature on ophthalmology reveals that at different times this subject has received the serious consideration of many leading men, among whom are some of our pioneers in ophthalmic surgery such as Desmarres, Sr Terrien, Vacher Panzer Bajardi, Lundsgaard, Cridland, and Harrison Butler We would not hope to add any new principle in ophthalmic surgery but only to develop a method of procedure that would utilize the possible factors that make for security and speedy recovery I shall try to describe this method in a few words.

With special conjunctival fixation forceps, the conjunctiva and subconjunctival tissues are grasped firmly above the cornea and extending from 4 millimeters above the limbus to the region of the equator The bridge should be about 12 millimeters in width and should have sufficient subconjunctival tissue to insure strength and nutrition. With the forceps, upward traction is exerted on the globe. This gives perfect fixation of the eyeball and at the same time reduces the tension which is desirable in preventing the iris from falling forward on the knife during the transfixion. In steadying the eye, this technique does not tend to make the incision open or gape as is often the case when pressure is applied below the cornea. In fact the effect is similar to that of a superior rectus suture but is more manageable in determining the direction and extent of its action

Moreover the vertical fold of the conjunctiva above the cornea held in the grasp of the fixation forceps facilitates the formation of the desired bridge by the cataract knife after it emerges through the sclerocorneal incision. The bridge can be made wholly with the knife, or it can be supplemented with scissors, or it can be fashioned entirely before the incision is made, or it can be modified, broadened, and shortened in glaucoma cases. The procedure will be more accurate if the knife incision includes only the upper third of the limbus arc, the wound being extended on either side with scissors so as to include a narrow band of conjunctiva 1 millimeter in breadth.

A matter of considerable importance relates to the judicious handling of the bridge, which can be used in all forms of cataract operations as well as in the various operations for glaucoma. I have endeavored in many ways to regulate the influence of this bridge upon the size and pliability of the sclerocorneal opening If a good bridge is fashioned, left alone, and the patient is directed to look down, the value of the bridge is, in a measure, nullified because the bridge tightens down on the globe and closes rather firmly the opening through which the lens must pass. If the patient looks straight forward, the lips of the sclerocorneal wound still remain in apposition. Therefore, the bridge must be elevated by some means in order to gain the adequate space desired. If the bridge is elevated by any kind of hook, both the corneal and the bulbar segments of the bridge will be rendered equally taut and there will be imparted to the incision a certain rigidity which is incompatible with facility in the lens delivery If the bridge is lifted by means of a thread passed under it, the same conditions of tension are produced By each of these procedures, the bridge can be drawn aside so as to give free access to the iris for iridectomy or iridotomy but the objectionable feature of rigidity is still maintained which favors rupture of the capsule at the moment of the delivery of the lens

There is, however one procedure which will

secure perfect relaxation of the corneal segment of the bridge with perfect access to the iris and lens and with the minimum of rigidity This is accomplished by taking into account the marvelous elasticity and extensibility of the bulbar conjunctival membrane, as is done in pterygium operations It is made in this way With special conjunctival bridge control forceps the entire bridge is grasped firmly at a point opposite the insertion of the superior rectus tendon and the bridge is dragged forward so that it folds over the cornea in a perfectly relaxed condition, or can be elevated to any desired extent whenever the occasion demands it, or can be drawn in any direction necessary adequately to expose the iris and lens, and yet without introducing the factor of rigidity Moreover, with the firm grasp of the upper bulbar segment of the bridge with its connecting epibulbar fibrous tissues, the downward rotation of the eye ball which can be steadied now in any required position, is permitted

Thus we command the doorway to the interior of the globe, and this we can open or close at will, thus facilitating the necessary instrumentation under direct inspection and affording at the same time immediate closure of the wound if any untoward complications should threaten or develop

The very instant that the lens is delivered, the lids can be closed and the eye ball can be left in its normal relations, these being the conditions most favorable for its safety Then, after a little period of rest, if needed, the toilet of the eye can be given any attention which may be indicated No stitches are to be inserted and removed. No inversion or eversion or maladjustments of flaps are possible The nutrition of the cornea is not even for one moment interrupted and the process of healing can proceed with accuracy and without delay By these measures, we are able to secure the greatest possible protection against infection, hemorrhage, vitreous loss, delayed union, iris prolapse, epithelial proliferation in the anterior chamber Thus we are able also to secure the minimum detention in the hospital and the greatest comfort and freedom throughout the period of recovery

SURGICAL TREATMENT OF STRABISMUS IN RELATION TO ORTHOPTIC TRAINING[1]

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THE subject of orthoptic training is of interest to all doing ophthalmic surgery. We are at present in the midst of another cycle or revival of this form of treatment for strabismus and heterophoria. Unlike previous cycles, however, I believe that this time orthoptic training has come to stay because it is being carefully evaluated and established on a firm scientific basis.

Surgical treatment of strabismus was originally designed mostly for cosmetic improvement. With advances in the differential diagnosis and surgical procedures, restoration of function seems to have become the dominant purpose in the treatment of strabismus. Orthoptic training seems to be the connecting link between cosmetic surgery and restoration of normal function or real cure.

In the general consideration of orthoptic training, the question naturally arises by whom and where it should be carried out. Inasmuch as it involves an understanding of psychology, physiology and pathology, and is quite closely related to surgical treatment, it seems to belong in the sphere of medicine, particularly ophthalmology. The ophthalmologist, however, already is a busy man. Can he find the time necessary to devote to this added burden? Not without assistance, I believe. Neither does it seem that this orthoptic treatment should be turned over to non-medical fitters of glasses who are untrained in the necessary fundamental sciences and who, without supervision, might exploit this very necessary form of treatment. The problem seems to have been solved by the development of carefully trained technical workers who carry out treatment under the supervision of, and in co-operation with, the ophthalmologist interested in the problem.

The question arises, of what value is orthoptic training? A careful review of the literature produces quite sufficient evidence to justify the opinion that orthoptic training is worth while in the treatment of strabismus. One has but to point to the contributions of Maddox, Pugh, Cantonnet, Fillioret and Beaumont abroad, and to the work of Wells, Berens, Hardy, Stark, Gunbor, Hicks, Hosford, and others in this country. In connection with the actual training, the question is often asked how long it should be continued. The answer, it appears, is that it should be continued as long as satisfactory and definite progress is being made. The value of orthoptic training in any given case cannot be established in a few months. In some of our most successful cases at the clinic, patients have been trained continuously for several years. One particularly successful result that I have in mind was obtained after 3 years of intensive training, during which there were periods of marked relapse. In selected cases and under favorable circumstances, training can be carried out from 3 to 5 years with good results. In most cases, however, operation should be performed much sooner than this, and further training should be given subsequently.

There is a natural tendency, once training is started, to hang on stubbornly past the point where surgery should be performed. I believe that early operation is indicated in many instances. The ideal procedure in any given case would seem to be a preliminary period of orthoptic training, then operation, and finally further training. Too often after a successful operation has been performed and the eyes appear to be straight, the family and the surgeon lose interest and further treatment is not given.

The objectives of orthoptics are seen as the overcoming of suppression, the avoidance of false projection, the development of simultaneous macular perception, fusion with amplitude, and finally stereopsis. Apparently no consideration is given to the limitations of treatment because of the patient's age. Cantonnet and Fillioret were of the opinion that it could be carried out successfully even up to the age of 35 years. Without doubt, however, the younger the patient when training is attempted, the better and easier are the results likely to be obtained.

In discussing some of the relationships between surgical treatment and orthoptic training, the question naturally arises as to when to operate. Savin might well have opened this discussion when he stated that surgical measures under modern conditions and with modern needles and instruments, could be carried out safely at any age over 3 years. He also thought that cosmetically successful operations should be followed by further orthoptic training. Griffith saw the pendulum swinging rapidly toward earlier operation when non-operative measures, reasonably tried,

[1]Presented before One of the Clinical Congresses, American College of Surgeons, San Francisco, October 28-November 2, 1945

failed to produce results Maddox (12) thought operation desirable when other measures seemed to have failed, and particularly if the time involved seemed to jeopardize the brain eye, and this regardless of the youthfulness of the patient His youngest patient was 16 months old So far, at the clinic, the youngest patient was 3 years old

Hine, while objecting to operating with the patient under general anesthesia because of difficulty in watching the eyes, felt that if treatment was delayed until after the age of 7 years, the chances for recovery would be remote The answer to this seems to be, "why delay so long?" Davis made the point that it was most important to effect a cure at a pre-school age by means other than with glasses, that is, by orthoptic training or operating, thus avoiding the mental trauma of strabismus and the wearing of glasses The age of the patient, then, no longer seems to be the determining factor in the problem of when to operate We must depend rather on the degree and nature of the strabismus, the condition of the visual apparatus, and the response or lack of response of the latter to training Feasibility and availability of the patient for training naturally must be considered

When large deviations have to be dealt with and there is no opportunity to try orthoptic training, it would appear sensible to straighten the eyes surgically and give parallelism a chance I have seen fusion develop spontaneously in both adults and children following operation when no training had been given Certainly this is better than merely to dismiss the patient with a pair of glasses Failure to respond in a reasonable length of time to refraction, occlusion, and orthoptic training, properly carried out and sufficiently tried, seems to be the prime indication for surgical intervention Just what constitutes a reasonable length of time seems in the light of present opinion to be 6 months to a year Surgery should be resorted to if there is a tendency to relapse from the point of view of either the strabismus or amblyopia, and also if excessive contracture of the muscles continues unabated and the opposing muscles appear to be weakening

In the persistently refractory case in which a vertical deviation is present, probably it is best in most instances to correct the vertical deviation surgically The eyes then will often proceed toward cure Having made progress up to a certain point with training, and then being unable to continue or sensing lagging interest on the part of the patient and his family, operation would seem to be the next step In high degrees of strabismus, after having obtained good vision and simultaneous perception by training, operation by reducing the angle of the strabismus would seem to save valuable time This is then to be followed by further training As Berens has said, it is important to operate in all cases in which the condition does not respond to non-operative measures and put the eyes in a position in which they may be able to respond Hine called attention to the group of strabismic patients whose eyes remain straight while stimulated by training, but which in the ordinary course of life return to their former state These patients, he felt, should be operated on

The indications for orthoptic training seem to be quite definite To determine in any given case whether surgical aid is necessary, orthoptic training should be tried as soon as vision is compatible with fusion Current opinion places this vision at about 6/12 At the clinic, however, we have 1 case in which fusion is perfect, with stereopsis, vision being 6/15 As a preliminary to operation, all agree that, where feasible, fusion training is essential The ability to possess simultaneous perception, corresponding retinal congruity, and some degree of fusion certainly insures a much brighter outlook for successful surgery After operation has been performed, the ensuing stage of muscular disorganization during which so frequently the patient is dismissed, would seem to be the time pre-eminently suited for the employment of orthoptic training Above all others, it is probably the time when there is the best chance of restoring normal function and ultimately bringing about a real cure Gifford called attention to the early intermittent evanescent type of strabismus in children In these cases, he believed that training should be started before the condition became established This appears to be a most excellent suggestion

False projection runs high in cases of alternating strabismus Pugh found it in 77 per cent of cases, but in my experience this seems rather high Alternating strabismus with false projection is, however, the least amenable to any form of treatment The argument against straightening alternating strabismus with false projection surgically is, of course, that persistent diplopia may result following operation In our experience at the clinic, alternating strabismus has been amenable, as a rule, both to training and surgery I have encountered temporary diplopia, lasting from a few days to several weeks, in many cases following operation Except in 2 instances, however, the diplopia finally disappeared and the result was satisfactory It seems probable that, when alternating strabismus with false projection

is corrected surgically one of several things may occur (1) there may be true projection and fusion at once, although this seems rather uncommon (2) there may be a period of disorganization, with gradual adjustment to some degree of fusion (3) there may be a condition of pseudobinocularism, or alternate suppression, which is probably the most common occurrence, and (4) there may be a continuation of the false projection with persistence of the diplopia. I believe this last occurs rarely If more patients with alternating strabismus were intensively trained after surgery the result might be surprisingly good.

Although discussion of the surgical procedures is not within the scope of this paper I expressed the point of view in a recent paper that possibly the best surgical results might be obtained after a very careful and refined differential diagnosis had been made, with selection from all the various surgical procedures of that combination best fitted for the case at hand.

In comparing the results of orthoptic training and operation in the treatment of strabismus, it would appear that one is as important as the other, and if to these forms of treatment are added proper occlusion and accurate refraction 4 weapons will be at hand for the combating of strabismus. It is difficult, indeed, to say which of the 4 is the most indispensable. The maximal results should be obtained through the combined use of all of them if properly performed and in correct sequence Operation should rarely be performed before refraction, occlusion, and orthoptic training have been given a reasonable trial On the other hand, one should not attempt to carry training past the point where it loses its effectiveness. When there are indications for surgical treatment, operation should be performed at once regardless of the age of the patient.

SUMMARY

Restoration of function seems to be the dominant purpose in the treatment of strabismus, and the connecting link between cosmetic surgery and restoration of normal function appears to be orthoptic training

Proper occlusion, accurate refraction, intensive orthoptic training, and selective surgery are the means at hand for the combating of strabismus All are of equal importance and the maximal results should be obtained through the combined use of all in proper sequence.

At the clinic, orthoptic training sufficiently and properly applied in selected cases has been of definite value in the treatment of strabismus

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A BRIEF CONSIDERATION OF THE HISTORY OF THE DEVELOPMENT OF MASTOIDECTOMY[1]

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ALTHOUGH really an otologic subject, mastoidectomy itself was developed to a very large degree by the work of a number of general surgeons It has seemed to me both proper and interesting to mention some of the factors regarding various developments which either antedated the actual mastoid surgery, or had no direct bearing upon it, but are important milestones in the history of otology Among these items is that of the aural speculum, the first use of the Eustachian catheter and first paracentesis of the drum membrane (myringotomy)

Although the employment of the aural speculum has been attributed to Guielmus Fabricius Hildanus (1560–1634), it is likely that the priority belongs to an earlier name, for Guy de Chauliac (1300–1368)—(the Father of Surgery) mentions the use of the ear speculum Systematic anatomical study which had remained almost in abeyance since the time of the Greeks, was revived in the 16th century by Vesalius (1514–1564), Eustachius (1510–1574), and Fallopius (1523–1562) This work was continued in the 17th and 18th centuries by men such as Valsalva (1666–1723), Morgagni (1682–1771), and Scarpa (1747–1832)

A non-medical man, the postmaster of Versailles, Edme-Gilles Guyot (1706–1786) endeavored to cure himself of impaired hearing by inflation of the tympanum by means of an instrument introduced through the mouth in the vicinity of the orifice of the Eustachian tube Paracentesis of the drum membrane (myringotomy) was apparently first carried out by the great English surgeon, Sir Astley Cooper (1768–1841) He observed several cases in which the drum membrane was perforated or destroyed without causing serious hearing impairment, and therefore, thought it probable that deafness due to Eustachian tube obstruction might be relieved by puncturing the tympanic membrane

With regard to the direct development of the actual operation on the mastoid process, it has been claimed by some that Ambroise Paré (1510–1590) was the first to perform mastoidectomy As a matter of fact, from all the evidence I can gather (and in this I am supported by Dr Frances R Packard whom I consider the authority on Paré in this country), Paré does not anywhere state that he even suggested operating on Francis II for his mastoid condition

The first successful mastoid operation for suppurative disease was performed in 1736 by Jean Louis Petit (1674–1750?), who was the foremost surgeon of his day Owing to various factors, not the least of which was the fatal result of the mastoidectomy performed on Baron Dr von Berger, physician to the King of Denmark, the operation fell into disrepute Two of the great English aural surgeons, William R Wilde (1815–1876) and Joseph Toynbee (1815–1866) were among those who also expressed themselves adversely with regard to the opening of the mastoid process It was due largely to Anton F von Troeltsch (1829–1890) that the German surgeons were stimulated to further work with reference to the mastoid operation Herman Schwartze (1837–1910) did a tremendous amount of work in connection with operation of acute cases of mastoiditis and did the first of this kind in Germany in 1863 The first mastoidectomy performed in the United States was by Lawrence Turnbull (1821–1900) He was born in England but lived most of his life in Philadelphia and there did most of his work The first mastoidectomy performed in England was by James Hinton (1822–1875) in 1868, and was reported in an address before the Royal Medical and Chirurgical Society in London

If there were intracranial complications in acute cases, or if chronic otitis media was present, it was found necessary to develop a more radical operation, namely the radical mastoidectomy This procedure was really the work of two general surgeons Ernst Kuester (1838–1930) and Ernst von Bergmann (1836–1907), both of whom presented the subject before the German Medical Society in 1888 and 1889 While Kuester was the first to remove the posterior wall of the bony canal, and Bergmann was the first to remove the outer bony wall of the attic, by their combined procedures the various cavities in the temporal bone, namely the antrum, attic, middle ear, and external canal were converted into one cavity Several modifications of the original Kuester-Bergmann operation were later developed E Zaufal (1837–1910) further modified the radical operation by working forward from the antrum to the attic, and by the incision of the upper and posterior portion of the membranous meatus Ludwig Stacke (1859–1918) advocated opening the mastoid bone from within outward After elevating the skin and periosteum from the posterior and superior walls of the bony canal, he first entered the tympanic cavity, then the attic, and finally the antrum Later various types of plastic flaps, skin grafting, etc. were developed, but the essential principles of the radical mastoid operation are still continued to the present time

[1]Abstract of paper presented before the Clinical Congress of the American College of Surgeons San Francisco, October 28–November 1, 1935

SURGICAL APPROACH TO THE NASAL ACCESSORY SINUSES[1]

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VARIOUS methods of surgical approach to the nasal accessory sinuses have been found useful in our practice.

In dental antritis, extraction of tooth followed by irrigation of antrum by the rhinologist, not by the dentist, we have found most satisfactory. The alveolar opening is allowed to close. If the irrigating fluid is still positive after 8 or 10 lavages, lipiodol may be installed. If there is present a filling defect and the secretion is still fetid, a radical antrum operation is given careful consideration. If no filling defect is present, the intranasal antrum operation may be the method of choice.

In cases in which the antrum cavity acts as a reservoir lipiodol will show no filling defect. In these cases the ethmoid cells are removed intranasally as well as the greater portion of the middle nasal antral wall but preserve the middle turbinate, if possible. If a filling defect is present, the antrum is explored before the intranasal ethmoid operation is done.

In polyposis, with the antrum and ethmoid cloudy, the radical antrum, intranasal ethmoid operation is indicated, if necessary the external ethmoid, frontal and sphenoid. The external frontal operation is done only as a last resort in many instances. The lipiodol test is usually not necessary inasmuch as the antrum is generally found to be involved in cases of polyposis with cloudy sinugram.

In the presence of dentigerous and other cysts of the antrum, the radical antrum operation is indicated.

When the nasal findings are negative, the sinugram negative and the lipiodol test shows no filling defect when the patient complains of fullness in the cheek, exploration of the antrum through the facial wall is the method of choice. In these cases we have many times found pathological changes in the recesses with edematous swelling of the mucous membrane in the region of the normal ostium.

In the presence of antrum suppuration, with no filling defect, the germs many times being anaerobic, the intranasal antrum operation is performed for ventilation.

In serous inflammation of the ethmoid, the intranasal ethmoid operation is used. The external operation may be done later if the patient is not relieved, and if the X ray film shows lateral prolongations of ethmoid cells into the roof of the orbit. Exploration of the antrum is carried out, if there is any doubt as to the presence of pathological changes in this cavity.

In suppurative ethmoiditis, the intranasal operation is done. If pus exudes from the nasofrontal duct at the time of operation the external frontal is immediately done. There is less danger of osteomyelitis as a complication if this is done.

If no pathological changes are found in the nose, if bulla ethmoidalis is noted in apposition with large uncinate cell causing closure of nasofrontal duct (vacuum headache) the intranasal frontal operation is performed.

At the time of the ethmoid operation, the region of the sphenoid should be examined. If this cavity is found diseased, or if the normal ostium is closed by thickening of the anterior wall, the sphenoid operation should follow. If the lining membrane of the sphenoid cavity is found involved, it is carefully removed.

In the presence of an upward displaced bifurcated cell causing closure of the nasofrontal duct and if it is impossible to open the nasofrontal duct satisfactorily in doing the intranasal operation the external ethmoid procedure may be indicated.

The radical external frontal operation is indicated when intranasal operative measures have failed to relieve patient of headache.

The radical frontal sinus operation is indicated in the presence of orbital, intracranial complications, or osteomyelitis.

In the fulminant type of infection, conservative means should be used for a few days, and if no relief is obtained the radical ethmofrontal operation should be done.

If "silent osteitis" is suspected in the alveolar region, a dental surgeon should be consulted. If the sphenoid bone is involved with osteitis, the entire anterior wall of sphenoid is removed. A latent osteitis of the frontal bone should not be operated upon unless symptoms demand.

A thorough analysis of each patient should be made before operative steps are undertaken, and an attempt must be made to determine which cell is the chief offender, or whether the discharge is originating from an involvement of a combination of cells. It cannot be too strongly emphasized that all sinuses found diseased should be surgically approached at the first operation, if possible.

[1] Abstract of paper presented before the Clinical Congress of the American College of Surgeons, San Francisco, October 28–November 2, 1928.

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THE RISK TO THE INFANT IN BREECH DELIVERY

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FOR a decade and a half the problem of fetal and neonatal mortality in breech delivery has been the subject of lively interest and discussion among obstetricians In 1926 Irving and Goethals (8) reviewed 10 years of experience with this problem at the Boston Lying In Hospital, and the present article is submitted as a detailed survey of the same subject covering twenty-two years in the same institution

DEFINITION OF TERMS

Since this article is intended to be a clinical study rather than a presentation of vital statistics in a bureaucratic sense and since it is concerned with all primary breech deliveries over a specified period stillbirths as well as neonatal deaths are included in the fatalities A *stillbirth* is defined as a newborn infant which never breathed after delivery, a *neonatal death* is a death which occurred after the establishment of independent respiration The term *gross mortality* is used to denote the ratio of total stillbirths and neonatal deaths to total deliveries in the series, it is also used to indicate the same ratio among the increments of premature, immature, and mature infants from which the entire series is derived *Crude mortality* is used to signify the incidence of stillbirths and neonatal deaths in each group into which the material is divided on any basis other than the maturity of the infant *Corrected mortality* is the term selected to express the combined stillbirth and neonatal death rate among infants which theoretically should have been born alive and should have survived *Neonatal mortality* in so far as the term is used in this paper mostly for purposes of comparison, expresses the ratio of neonatal deaths to living births in any given group or category, and may be computed as *gross crude* or *corrected*, in accordance with the definitions previously given

INCIDENCE OF BREECH DELIVERY

From January 1, 1913 to January 1 1935 30 655 patients were delivered on the house service of the Boston Lying In Hospital Of these, 1 219 women were delivered through the pelvis of 1 242 infants by the primary breech mechanism Those cases of abdominal cesarean section in which the breech presented at the time of operation regardless of whether the presentation was considered the essential or contributory indication for section are not included within the scope of this paper Otherwise all breech deliveries are reported, without regard to the time in gestation when labor occurred, consequently the series includes infants of all postconceptional ages and all birth weights from the obvious non-viability of miscarriage through the gradations of prematurity, to full term The total number of infants born includes those resulting from 23 labors in which each of a pair of twins presented by the breech

TABLE I—GROSS MORTALITY IN BREECH DELIVERY BY YEARS

	Deliveries	Well	Stillborn	Dead	Macerated	Malformations	Premature	Intra-uterine deaths	Mechanical deaths	Mortality %
1913		21	5	5	3		5			9.1
1914	27	24	3	3					3	20.7
1915	18	18	2	2					4	20.7
1916	43	39	6	8	4		6			23.3
1917	31	3	8		4		9	3		28
1918	34	21	6	6			3			23
1919	37		7	8			7	4		40.5
1920	39	34	8						4	23
1921	37	28		7			4		4	24.3
1922	36	30	3	3						16.6
1923	43	3	5	5					2	24.2
1924	30	27	9	4					3	26
1925	49	37	8	10	3		8	2		26
1926	79	54	13	12	3		8	6		21.6
1927	83	68	8	7			3		6	16
1928	69	53		4	4				6	16
1929	53	40	7	3			3		3	17
1930	100	78	13	13		6	4	6	3	26
1931	84	64	13	7	6		2		4	20.2
1932	66	48	9	9	7		2			19.5
1933	71	63	8	10		3	7		3	18
1934	80	65	12	8	3	4		3	6	22
	1,242	922	163	157	63	11	98	22	59	25.7

Breech delivery therefore, occurred in 3.97 per cent of all births during the 22 year period.

GROSS MORTALITY IN BREECH DELIVERY

Of the 1,242 infants delivered, 922 left the hospital alive 320 were discharged dead, of which 163 were stillborn and 157 died in the neonatal period The gross mortality therefore was 25.7 per cent, or stated in another manner there were 131 stillbirths and 126 neonatal deaths per thousand breech births. Figures are available for the years 1924 through 1934, corresponding exactly to the second half of the period covered by this survey which indicate that in the general incidence of all hospital deliveries 62 stillbirths and 22 neonatal deaths occurred in each thousand births (1) These comparative figures serve to show the marked increase in risk to which the infant is exposed *by the circumstance* of breech delivery

CLASSIFICATION OF CAUSES OF STILLBIRTHS AND NEONATAL DEATHS

Table I indicates the gross mortality in breech delivery at the Boston Lying In Hospital during the years covered by this survey To any student of birth fatalities, it soon becomes evident that cases tend to group themselves into various categories from a clinical standpoint *Thus, certain babies are stillborn following* intra-uterine death at some interval before labor occurs, and are therefore delivered in a state of maceration others are congenitally deformed some are born prematurely before any hope of "viability" can be expected certain others succumb to the mechanical hazards of the birth mechanism and a few are stillborn or die of the effects of accidental complications of birth or of conditions entirely unassociated with delivery Such a *grouping of* causes of death can be effected along clinico-anatomical lines with a fair de-

TABLE II.—STILLBIRTHS—CLINICAL DIAGNOSES FROM THE RECORDS

Clinical diagnoses	Total	Macerated	Malformation	Premature	Intercurrent death	Mechanical deaths
Macerated	55	55	0	0	0	0
Non-viable	10	3	0	0	5	2
Maternal toxemia	2	1	0	0	1	0
Maternal infection	1	0	0	0	1	0
Prematurity	3	0	0	0	1	2
Unspecified	18	1	0	0	9	8
Non-viable	8	2	3	0	3	0
Anencephalus	8	0	8	0	0	0
Anencephalus, spina bifida	1	0	1	0	0	0
Hydrocephalus	1	0	1	0	0	0
Hydrocephalus spina bifida	5	0	5	0	0	0
Congenital ascites	1	0	1	0	0	0
Congenital cystic kidneys	1	0	1	0	0	0
Congenital cyst of mesentery	1	0	1	0	0	0
Generalized dropsy	1	0	1	0	0	0
Multiple congenital anomalies	2	0	2	0	0	0
Asphyxia	36	0	0	0	9	27
Intra-uterine asphyxia	1	0	0	0	1	0
Intracranial hemorrhage	1	0	0	0	0	1
Difficult delivery	1	0	0	0	0	1
Died, difficult delivery (stillborn)	2	0	0	0	1	1
Died, non-viable (stillborn)	4	1	0	0	3	0
	163	63	24	0	34	42

gree of accuracy and tends not only to give a comprehensive view of the fatalities in the series but also to point the way to the computation of corrected mortality For this reason the 22 diagnoses of stillbirth, listed in Table II, and the 19 diagnoses of neonatal death, computed in Table III, have been condensed into 5 categories or groups, defined as follows

1 Maceration This signifies antepartum intra-uterine death and decomposition, regardless of causation Obviously all deaths in this category are stillbirths

2 Malformation This signifies gross and tragic anatomical deformities incompatible with life or continuance of life, for which, aside from religious grounds, destructive operations are generally approved About two-thirds of the deaths in this category were stillbirths, while the remainder occurred in infants born alive

3 Prematurity The diagnosis of death from prematurity is, at best, unsatisfactory Evidence accumulating year by year indicates that many, if not the majority, of infants who die of "prematurity" actually succumb to intracranial or other birth traumas Therefore in our classification of deaths, we have admitted prematurity as a diagnosis only in the absence of clinical or autopsy evidence of mechanical causation All dead infants in this category were born alive

4 Intercurrent deaths In these cases stillbirth or neonatal death occurred from antepartum infarction, infection, or separation of the placenta, from prolapse of the cord before labor or early in the first stage, from mismanagement of the labor outside the hospital in other hands before admission, from such anomalies, undiagnosable antepartum, as congenital heart lesions, and from incidental diseases which were present in the infant in early neonatal life

5 Mechanical deaths In this category stillbirth or neonatal death during or following the act of delivery occurred from asphyxia or trauma, demonstrable either clinically or at postmortem In this group occur the cases of intra-uterine asphyxia, intracranial hemorrhage, and difficult delivery recorded in the histories, as well as many instances of "prematurity" and unspecified causation It is in this category that a search for poor obstetric judgment and for mismanagement of labor would find its greatest return

TABLE III.—NEONATAL DEATHS—CLINICAL DIAGNOSES FROM THE RECORDS

Clinical diagnosis	Total	Macerated	Malformed	Premature	Intercurrent deaths	Mechanical deaths
Malnutrition						
Bronchopneumonia						
Congenital heart	3				3	
Congenital heart and bronchopneumonia					1	
Hemorrhagic diathesis						
Anencephalus						
Congenital hernia, navel cord						
Congenital diaphragmatic hernia (Fascione)			1			
Hydrocephalus	1		1			
Hydrocephalus, congenital syphilis						
Hydrocephalus, spina bifida						
Meningocele						
Prematurity	95			86		
Non viable	8			4		
Difficult delivery						1
Traumatic rupture of umbilical cord						
Intracranial (cerebral) hemorrhage	18					18
Unspecified	10		6			
	1			97	12	19

Study of the individual records and diagnoses of death, correlated with the classifications of death in Tables II and III indicates a reasonable accuracy of such correlation in most instances Thus stillbirths and deaths from asphyxia, intracranial (cerebral) hemorrhage, difficult delivery etc fall naturally into the mechanical group for the most part, *with a few in the intercurrent classification* The macerated and malformed infants are grouped automatically The diagnosis of prematurity as a cause of stillbirth is not admitted in the groupings, and non viable stillbirths *are found in all cases to be accounted for by* reasons other than prematurity Neonatal deaths from 'prematurity are found to be due to mechanical or intercurrent causation in *7 5 per cent* of the cases so diagnosed The intercurrent deaths prove *the hardest of all to* classify while 14 of the 51 were due to unpredictable complications such as maternal toxemia or infection antepartum, and atelectasis bronchopneumonia congenital heart, and hemorrhagic diathesis postpartum the balance including accidents of labor of one sort or another might with some justification, be considered as mechanical on the other hand death might well not have occurred but for the fortuitous complication, and the inclusion of such cases in the intercurrent category seems indicated

Postmortem examination is recorded in 39 of the 320 fatal cases, an incidence of 12 1 per cent One macerated fetus was thus examined, and three monstrosities One infant in the premature category came to autopsy as did 6 who died of intercurrent causes, and 28 of the 79, or 35 4 per cent, who succumbed to mechanical conditions While in the last named group confirmatory anatomical evidence of birth trauma or of asphyxia was found in all cases, it must be conceded that the series is disappointing in its lack of postmortem data on infants classed as dying of prematurity

THE FACTOR OF PREMATURITY AND ITS BEARING ON FETAL AND NEONATAL MORTALITY

Gross mortality among premature infants It has already been noted that all infants born by the *primary breech mechanism* are recorded in this series regardless of the stage of gestation in which labor occurred Some,

TABLE IV—GROSS MORTALITY IN BREECH DELIVERY, BY BIRTH-WEIGHTS

Pounds	Deliveries	Well	Stillborn	Died	Macerated	Mal formation	Premature	Intercurrent deaths	Mechanical deaths	Mortality %
0 —1	3	0	3	0	3	0	0	0	0	100 0
1 —1½	12	0	9	3	4	0	3	4	1	100 0
1½—	16	0	6	10	1	2	8	4	1	100 0
2 —2½	28	1	13	14	7	3	12	3	2	96.4
2½ —3	31	4	8	19	4	1	18	4	0	87 0
3 —3½	40	7	10	23	3	2	19	3	6	82 5
3½—4	37	20	6	11	1	1	9	2	4	45 9
4 —4½	42	23	7	12	4	1	9	3	2	45 2
4½—5	37	24	5	8	2	2	8	1	0	35 1
5 —5½	69	57	6	6	2	2	2	2	4	17 3
5½—6	77	65	6	6	1	3	1	1	6	15 5
6 —6½	135	121	6	8	1	1	0	3	9	10 3
6½—7	117	101	9	7	2	4	0	3	7	13 6
7 —7½	160	144	8	8	1	1	0	2	12	10 0
7½—8	139	130	6	3	1	3	0	1	4	6.4
8 —8½	103	93	2	8	0	1	0	2	7	9 7
8½—9	72	66	4	2	0	1	0	0	5	8 3
9 —9½	44	36	5	3	1	0	0	2	5	18 1
9½—10	18	14	4	0	0	1	0	1	0	22 2
Over 10	24	16	8	0	5	0	0	1	2	33 3
Not recorded	38	0	32	6	20	6	3	7	2	100 0
	1,242	922	163	157	63	35	92	1	79	25 7

therefore were premature and it will be well, before discussing the effect of prematurity on mortality, to define the term Length of gestation as reckoned from the date of the last menstrual period is the usual criterion adopted in determining maturity of the fetus *in utero* but in any considerable series of cases gleaned from records this standard is frequently untrustworthy For this reason we have chosen to consider the birth weight of the infant as a more reliable standard, and accordingly classify an infant weighing less than 5 pounds at birth as premature, one weighing over 5 but less than 6 pounds as immature, and one who weighs 6 pounds or over as mature

It is a matter of general observation that breech presentation is much commoner in pregnancy before the last weeks of gestation than at term Hence, should labor supervene spontaneously or be induced artificially at any time previous to the tenth lunar month it is reasonable to expect a higher incidence of breech presentation in premature labors than in deliveries at term Conversely, a given series of breech deliveries should, *a priori*, yield a higher ratio of premature infants than the general ratio of premature to mature infants in the newborn clinic population

Arranging the infants in our breech series according to birth weights we find in Tables IV and V, that 246 were premature 146 immature, 812 mature and 38 not weighed The gestational dates in the 38 cases in which weights were not recorded are as follows 4 to 5 months 1, 5 to 6 months, 5, 6 to 7 months, 9, 7 to 8 months, 10, 8 to 9 months, 5, at term, 7, information lacking, 1 From these figures one may compute the incidence of prematurity in the series either as 246 cases in 1,204 *weighed* infants, or 20 4 per cent, or, considering as premature all unweighed infants below 8 months as 271 of 1 242 babies delivered, or 21 7 per cent Whichever of these figures one prefers they are both more than three times as high as the 6 per cent (1 4) incidence of prematurity in the hospital deliveries at large

TABLE V —GROSS MORTALITY IN BREECH DELIVERY AMONG PREMATURE, IMMATURE, AND MATURE INFANTS—INCIDENCE OF PREMATURITY

	Deliveries	Well	Stillborn	Dead	Macerated	Malformation	Premature	Intracranial deaths	Mechanical deaths	Mortality %
Premature, by weight	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		[illegible]	[illegible]	[illegible]	[illegible]
Premature, unweighed	[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		[illegible]
Immature, by weight	[illegible]				[illegible]	[illegible]	[illegible]		[illegible]	[illegible]
Immature, unweighed	[illegible]		[illegible]		[illegible]					[illegible]
Mature, by weight	[illegible]	[illegible]	[illegible]	[illegible]				[illegible]	[illegible]	
Mature, unweighed	[illegible]		[illegible]		[illegible]					[illegible]
Maceration unrecorded, unweighed					[illegible]					[illegible]
Total deliveries, by weight	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total deliveries, unweighed	[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		[illegible]
Total deliveries	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Incidence	By weight, %	Total deliveries, %
Premature infants	[illegible]	[illegible]
Immature infants		
Mature infants	[illegible]	[illegible]

The gross mortality in premature infants in this series may be reckoned either as 167 stillbirths and deaths in 246 premature infants delivered, or as 192 fatalities in 271 deliveries The gross mortality therefore is either 67 8 *per cent* or 70 4 *per cent* *Eliminating* the stillborn, the neonatal death rate amounts to 55 8 per cent or 56 8 per cent respectively in the weighed and total groups These figures are considerably in excess of the 38 per cent neonatal death rate among prematures in the hospital at large for the period 1923 through 1933 (4)

Table IV indicates that among premature breech born infants, stillbirths and neonatal deaths claim more than 50 per cent of those weighing less than 3 pounds 8 ounces The neonatal death rate among live born infants is also in excess of 50 per cent below this birth level (Table VI) That the same mortality holds in general for newborn prematures is also shown in Table VI (6) When, however the weight of the infant exceeds this figure the risk of birth decreases much more rapidly with increasing poundage in infants in general than in those born by the breech.

The conclusions to be drawn from our figures concerning the incidence of prematurity in breech born babies, and from the gross mortality in this group may be expressed as follows

1 Prematurity occurs at least three times as frequently in infants born by the breech as in newborn infants in general

2 Three pounds and 8 ounces is the minimum weight level at which a premature newborn has an even chance of survival whether born by the breech or any other mechanism

3 Breech delivery of premature infants is associated with a higher mortality in weight groups above the 3 pound 8 ounce level than is to be found in delivery of premature infants in general in similar weight groups

4 Not only is prematurity an important factor in the gross mortality of breech born babies breech birth is an equally important factor in the mortality of premature babies

Gross mortality among immature infants. In this series 146 babies weighed between 5 and 6 pounds at birth Twelve were stillborn and 11 died in the neonatal period The gross mortality was therefore 16 4 per cent of weighed infants, and the neonatal mortality was 8 9 per cent of babies born alive If we arbitrarily assume *that the 5 unweighed infants* born between 8 and 9 months were immature the figures are respectively 19 2 per cent and 10 2 per cent. Since general neonatal mortality for immature infants in the years 1932 and 1933 was 3.1 per cent (6) it is evident that breech presentation increases the risk of birth for the immature infant approximately threefold

Gross mortality among mature or full term infants The total series of breech born infants includes 812 which, by weight were classified as mature, together with 7 full term babies whose birth weights were not recorded Of the weighed babies, 52 were stillborn, and 39 died neonatally, of those not weighed, all were stillbirths The gross mortality was therefore 11 2 per cent or 11 9 per cent, and the neonatal death rate 5 1 per cent Since the last named rate in the hospital at large is about 0 7 per cent (6), it would seem that the risk of birth for breech infants is increased at least seven times by the occurrence of such presentation

Returning to Table IV one sees a strikingly consistent downward curve in gross mortality by weight groups to a minimum at 7½ to 8 pounds, interrupted by a paradoxical irregularity between the 5½ and the 7 pound groups which may be due to an accidentally low mortality in the 6 pound, or an accidentally high mortality in the 6½ pound group [1] From the minimum gross mortality of 6 4 per cent among babies weighing from 7½ to 8 pounds, the mortality increases consistently in the groups above this level Offhand one would suppose that the increasing size of the fetus would account for the increased risk on a mechanical basis, but in the highest weight groups, from 9½ pounds on, the recorded mortality is due more often than not to maceration, malformation, or to intercurrent causes

A general and comparative tabulation of gross fetal and neonatal mortality in breech born infants Table VII is inserted at this point to show the gross antenatal, natal and neonatal death rates in the breech series from 1913 through 1934, parallel with corresponding figures for all hospital deliveries from 1924 through 1934 [1] The strikingly higher incidence of stillbirths and neonatal deaths among breech born infants as contrasted with the occurrence of fatalities among the hospital newborn population at large is evident in both premature deliveries and immature and mature births

[1] A statistician's delight in a smooth curve might be somewhat dampened by this finding, but he might find solace in a belief that if the 7 unweighed but presumably mature infants happened to fall in the 6 pound group the mortality of which would then be 14 7 per cent, the regularity of the curve would be restored.

TABLE VI —GROSS NEONATAL MORTALITY AMONG PREMATURE BREECH BORN INFANTS CONTRASTED WITH SIMILAR MORTALITY AMONG ALL PREMATURE INFANTS BORN IN THE HOSPITAL

Weight in pounds	1913–1935 Breech series			1923–1934 General series		
	Deliveries	Deaths	Mortality %	Deliveries	Deaths	Mortality %
Less than 1	0	0	0	1	1	100
1—1½	3	3	100	9	9	100
1½–2	10	10	100	33	32	97
2 –2½	15	14	93 3	61	55	90
2½–3	23	19	82 6	84	58	69
3 –3½	30	23	76 6	112	67	59 8
3½–4	31	11	35 4	143	46	32 2
4 –4½	35	12	34 2	230	45	19 6
4½–5	32	8	25 0	262	29	11 1
	179	100	55 8	935	342	38

THE EFFECT OF COMPLICATIONS OF PREGNANCY, LABOR, AND DELIVERY UPON MORTALITY AMONG BREECH BORN INFANTS

The figures so far recorded include all breech deliveries through the pelvis over a period of 22 years It cannot be said that in all cases pregnancy and labor were normal so that the gross mortality among the infants born was due to the mechanics of birth; on the contrary 272 of the infants born were exposed at some time *in utero* or *intrapartum*, to one or several complicating factors which in themselves are generally recognized as dangerous to the life of the fetus before or during birth Though these conditions, as they occurred, are recognized and will be recorded herewith, the number of cases occurring under each heading is in most instances too small to make a thorough analysis of the prematurity factor, etc, worth while However, it should be pointed out that when such a condition co-exists with breech presentation the mortality risk should be compared *not only with the risk incurred by an infant breech born of a mother free of such complication but also with the risk incurred by any infant born of a mother in whom such complication is present* Thus, the breech born infant of an eclamptic mother is subjected to the combined risks of maternal eclampsia and of breech de-

TABLE VII—GROSS ANTENATAL, NATAL, AND NEONATAL DEATHS IN BREECH DELIVERY CONTRASTED WITH ALL SUCH DEATHS OCCURRING IN THE HOSPITAL (EXPRESSED IN THE RATE PER THOUSAND BIRTHS)

		[illegible] through [illegible]	[illegible] through [illegible]	[illegible] through [illegible]	[illegible] through [illegible]	[illegible] through [illegible]	[illegible] through [illegible]
Gross death rate	Hospital series				[illegible]	[illegible]	[illegible]
	Breech series	[illegible]	[illegible]	[illegible]			[illegible]
Miscarriages, premature and non-viable stillbirth rate	Hospital series				[illegible]	[illegible]	[illegible]
	Breech series	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Viable infant stillbirth rate	Hospital series				[illegible]	[illegible]	[illegible]
	Breech series	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Premature infant neonatal death rate	Hospital series				[illegible]		
	Breech series		[illegible]	[illegible]	[illegible]		[illegible]
Immature and full term infant neonatal death rate	Hospital series					[illegible]	[illegible]
	Breech series	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Total births	Hospital series				[illegible]	[illegible]	[illegible]
	Breech series	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

livery that born of a woman with placenta previa runs the risk of death from both breech delivery and the effects of antepartum hemorrhage and asphyxia For these reasons the complicated breech deliveries are arranged in Table VIII the analyses of separate complications are shown with the mortality in each

1 Pre eclamptic toxemia alone was present in the mothers of 105 of the infants delivered Eleven other babies were born of toxemic patients in whom further complications occurred, such as syphilis, pyelitis, cardiac disease placenta previa ablatio placentæ and prolapse of the cord

2 Eclampsia was a complication in 13 of the patients delivered

TABLE VIII—CRUDE MORTALITY IN BREECH DELIVERY IN CASES COMPLICATED BY PATHOLOGICAL PREGNANCY OR LABOR, TABULATED ACCORDING TO COMPLICATION RECORDED

	Complication	Cases	Well	Deaths	Mortal ity
	Pre eclamptic toxemia	[illegible]	[illegible]	[illegible]	[illegible]
	Pre eclamptic toxemia complicated			[illegible]	[illegible]
	Eclampsia				[illegible]
	Chronic nephritis	[illegible]			[illegible]
	Chronic nephritis, complicated				[illegible]
	Syphilis		[illegible]	[illegible]	[illegible]
	Cardiac disease	[illegible]			[illegible]
	Cardiac disease complicated				[illegible]
6	Diabetes	[illegible]			[illegible]
7	Hydramnios	[illegible]		[illegible]	[illegible]
	Hydramnios complicated				[illegible]
8	Ablatio placentæ	[illegible]		[illegible]	[illegible]
	Ablatio placentæ complicated				[illegible]
9	Placenta previa	[illegible]		[illegible]	[illegible]
	Prolapse of the cord	[illegible]			[illegible]
	Miscellaneous	[illegible]	[illegible]		
		[illegible]	[illegible]	[illegible]	[illegible]

3 Chronic nephritis complicated 16 deliveries in one other ablatio placentæ was superimposed upon the kidney lesion.

4 Eleven deliveries were in syphilitic patients

5 In 13 deliveries cardiac disease was a complicating factor One additional cardiac developed hydramnios

6 Diabetes mellitus was present in 5 patients

7 Hydramnios was present in 7 cases, and in one other was associated with placenta previa

8 Ablatio placentæ in addition to the cases here in reported occurred 27 times In 2 other patients this condition was complicated by prolapse of the cord

9 Placenta previa alone occurred in 10 cases

10 Prolapse of the cord alone occurred in 32 deliveries

11 Miscellaneous complications occurred in 17 cases. acute bronchitis, chorea cystitis, epilepsy fibroid uterus, hydronephrosis, peritonitis, 1 each bronchitis associated with cystitis, 1 pyelitis, 3 pyelitis and cholecystitis, 1 pulmonary tuberculosis, 3

The figures in Table VIII indicate that crude fetal and neonatal mortality in breech delivery occurring in pathological pregnancy or labor is from 33 per cent to 300 per cent higher than the gross mortality in breech delivery in general and that it is increased to between three and nine-fold that occurring in uncomplicated delivery (cf Table VI) Since the various complications are represented by small groups, and since they differ so fundamentally from each other the tabulation of crude mortality by years and by birth weights yields no significant information

TABLE IX—CRUDE MORTALITY IN COMPLICATED BREECH DELIVERY, AMONG PREMATURE, IMMATURE, AND MATURE INFANTS—INCIDENCE OF PREMATURITY

	Deliveries	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Mortality %
Premature by weight	106	21	46	39	19	2	33	22	0	80 1
Premature, unweighed	12	0	11	1	5	2	1	4	0	100 0
Immature by weight	42	3	5	5	3	1	0	1	3	23 8
Immature, unweighed	4	0	2	2	2	0	0	1	1	100 0
Mature, by weight	106	78	18	10	4	4	0	5	15	26 4
Mature unweighed	2	0	2	0	2	0	0	0	0	100 0
Total deliveries by weight	254	131	69	54	26	7	33	30	27	48 4
Total deliveries, unweighed	18	0	15	3	0	2	1	5	1	100 0
Total deliveries	272	131	84	57	35	9	34	35	28	51 8

Incidence	By weight, %	Total deliveries %
Premature infants	41 7	43 3
Immature infants	16 5	16 9
Mature infants	41 7	39 7

other than that shown in Table IX which summarizes the incidence of premature, immature, and mature deliveries and the crude mortality in each grade The incidence of 43 3 per cent of premature infants in this group is to be expected since not only do many of the complications, such as chronic nephritis and syphilis, predispose to premature labor, but others such as toxemia and placenta prævia, often require termination of pregnancy a considerable time before term Table X (7) shows that the dangerous complications of placenta prævia ablatio placentæ, and prolapse of the cord are not only three, five, and five times, respectively as frequently associated with breech presentation as with pregnancy and labor in general but are also in each instance productive of a higher mortality among the newborn

FETAL AND NEONATAL MORTALITY IN SIMPLE OR UNCOMPLICATED BREECH DELIVERY

The preceding paragraphs have demonstrated the tremendously increased risk to the infant in breech delivery in cases in which pathological pregnancy or labor co-exists Analysis of 970, or 78 1 per cent of the deliveries in this series, in which pregnancy and labor were free of the dangerous complications herein mentioned, indicates that crude mortality among the newborn was 18 5 per cent, a figure appreciably lower than the gross mortality among all deliveries This group of uncomplicated deliveries is presented in Table XI which shows in marked contrast to the figures from Table IX, that

1 The crude mortality in the group was 18 5 per cent

2 The incidence of premature infants was 15 7 per cent

3 Of the premature infants 62 1 per cent failed to survive

4 In the immature category 14 2 per cent were stillborn or died

5 Mature infants showed a crude mortality of 9 5 per cent

Table XII shows crude mortality among infants in this group by birth weights The curve obtained is less regular than that shown in Table IV, but is in general similar to it with the same sharp fall in mortality between the 3 and 3½ pound groups

TABLE X—INCIDENCE OF PLACENTA PRÆVIA ABLATIO PLACENTÆ AND PROLAPSE OF THE CORD FOUND IN BREECH DELIVERY AND IN GENERAL

Breech deliveries

Patients delivered with		All patients delivered	Incidence %	Mortality %
Placenta prævia	22	1219	1.8	81.8
Ablatio placentæ	31	1219	2 5	74 [illegible]
Prolapse of the cord	29	1219	2 3	55 1

General consecutive deliveries

Patients delivered with		All patients delivered	Incidence %	Mortality %
Placenta prævia	228	39 184	0 58	57.9
Ablatio placentæ	128	26 731	0.47	61 5
Prolapse of the cord	335	67 761	0.49	40 0

TABLE XI.—CRUDE MORTALITY IN UNCOMPLICATED BREECH DELIVERY AMONG PREMATURE, IMMATURE, AND MATURE INFANTS—INCIDENCE OF PREMATURITY

	Deliveries	Well	Still born	Dead	Monstrosities	Malformations	Premature	Intracranial deaths	Mechanical deaths	Mortality %
Premature, by weight	[illegible]	[illegible]	[illegible]	6	[illegible]	[illegible]	[illegible]		7	[illegible]
Premature, unweighed	3		[illegible]	3	6					[illegible]
Immature, by weight	[illegible]	[illegible]	7	7		4	3		7	[illegible]
Immature, unweighed										[illegible]
Mature, by weight	[illegible]	[illegible]	[illegible]	[illegible]	7	8			[illegible]	[illegible]
Mature, unweighed	[illegible]		[illegible]		3					[illegible]
Maturity unascertained unweighed										[illegible]
Total deliveries, by weight	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		[illegible]	[illegible]	[illegible]	[illegible]
Total deliveries, unweighed	[illegible]		[illegible]	3						[illegible]
Total deliveries	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Incidence	By weight, %	Total deliveries, %
Premature infants	[illegible]	[illegible]
Immature infants	[illegible]	[illegible]
Mature infants	[illegible]	[illegible]

Crude mortality in uncomplicated breech delivery will be further discussed later in this article in its relation to corrected mortality *in the same group of cases.*

CORRECTED FETAL AND NEONATAL MORTALITY IN BREECH DELIVERY

In computing corrected statistics in a *review of mortality* the writer is forced to abandon the objectivity of reported figures for a more or less vulnerable position in which opinion must guide him in reaching his conclusions. The present paper is no exception to this rule. From this it follows that the corrected mortality figures of one observer may differ markedly from those of another due to a difference of premises in making the corrections. For example, King and Gladden, in computing their corrected mortality exclude cases of babies under 5 pounds, macerated infants, and multiple pregnancies. Caldwell and Studdiford in their report omit macerated infants and others under 4 pounds in weight. Taussig deducts macerated fetus, premature infants, twins, and malformations in arriving at his conclusions, but includes one death complicated by prolapsed cord in a case delivered of a pre-eclamptic mother and another complicated by ablatio placentæ. Mohler in computing a traumatic death rate in breech delivery excludes infants under 3 pounds, premature and macerated infants, and certain others over 3 pounds in weight. Morton assumes 1,500 grams or 3 pounds, 5 ounces, as the lower limit of viability in the newborn child, and includes only babies above that level in reporting his series. He calls attention *however to the difference in prognosis* for "viable" infants below and above 2,500 grams, or 5 pounds, 8 ounces. Cannell and Dodek, who include 13 cases delivered by cesarean section in a series of 562 breech infants, exclude premature infants under 5 pounds 8 ounces, malformations, and macerated fetus, in correcting their gross figures.

This brief summary of methods of correcting gross mortality figures used by various American authors indicates that their respective statistics are not founded upon any common denominator and hence are not strictly comparable. The present article at least suggests a common denominator not only by separating the pathological from the uncomplicated pregnancies and labors, but also by separating the premature from the immature and mature infants delivered. Any interested reader who may be so inclined provided only that he use the English rather than the metric system of birth weights, will find in the accompanying text and tables ample material which he may use to compare with his own figures.

TABLE XII—CRUDE MORTALITY IN UNCOMPLICATED BREECH DELIVERY, BY BIRTH WEIGHTS

Pounds	Deliveries	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Mortality %
0–1	0	0	0	0	0	0	0	0	0	0 0
1–1½	2	0	0	2	0	0	2	0	0	100 0
1½–2	6	0	1	5	0	1	5	0	0	100 0
2–2½	14	1	5	8	3	3	7	0	0	92 8
2½–3	17	3	2	12	2	1	11	0	0	82 3
3–3½	22	3	5	14	1	2	11	1	4	86 3
3½–4	24	15	3	6	1	1	5	0	2	37 5
4–4½	29	18	3	8	2	1	6	1	1	37 9
4½–5	26	18	2	6	1	1	6	0	0	30 7
5–5½	43	39	2	2	0	1	2	0	1	9 3
5½–6	67	51	5	5	0	3	1	0	6	16 3
6–6½	115	106	4	5	0	1	0	3	5	7 8
6½–7	95	88	2	5	0	2	0	2	3	7 3
7–7½	138	126	6	6	1	0	0	2	9	8 6
7½–8	128	110	6	3	1	3	0	1	4	7 0
8–8½	94	88	1	5	0	1	0	0	5	6 3
8½–9	66	62	2	2	0	1	0	0	3	6 0
9–9½	37	29	5	3	1	0	0	2	5	21 6
9½–10	12	11	1	0	0	0	0	1	0	8 3
Over 10	21	14	7	0	4	0	0	1	2	33 3
Not recorded	20	0	17	3	11	4	2	2	1	100 0
	970	791	79	100	28	26	58	16	51	18 5

The standard selected for correcting crude mortality in this series is a simple one, e g, the elimination of all cases in which macerated or grossly malformed infants were born These categories alone, it seems to the writer, may be safely disregarded, since no amount of obstetrical skill and judgment in the management of labor can prevent either maceration or malformation The 3 other groups should be included, for the following reasons

1 Neonatal deaths from "prematurity" must occur in any series in which labor ensues before term Naturally, as the present series shows, no mature baby dies of "prematurity," but many premature infants do, and a few immatures may Clifford (5) has called attention to the risk to the premature infant of delivery by various methods, and it may be that the mechanical stress of breech delivery causes more deaths of premature infants than "prematurity" itself

2 Stillbirths and neonatal deaths from mechanical factors have been shown to occur among premature immature, and mature newborns Asphyxia, intracranial injury, and injuries of the cord comprise the bulk of such fatalities, as a result of which obstetrical judgment and the management of delivery are on the defensive when these cases are considered

3 Stillbirths and deaths of intercurrent causation have been discussed to some extent previously Some are due to intercurrent disease of the newborn, and hence are unpredictable Others, though based on the mechanics of labor and delivery, are purely accidental, as illustrated by the case of the multipara who arrives at the hospital with the legs, buttocks, and trunk of the infant born but with the shoulders and head still imprisoned in the birth canal Corrected statistics should be made accountable for such fatalities though not necessarily *responsible* for them

TABLE XIII—CORRECTED MORTALITY IN UNCOMPLICATED BREECH DELIVERY FOR PREMATURE, IMMATURE, AND MATURE INFANTS

	Premature	Immature	Mature	Total
Deliveries	135	100	691	926
Well	55	90	648	791
Stillborn and died	67	10	45	125
Premature	55	3	0	58
Intercurrent deaths	4	0	12	16
Mechanical deaths	8	7	36	51
Mortality per cent	33 6	10 0	6 9	13 6

TABLE XIV —CRUDE AND CORRECTED MORTALITY IN UNCOMPLICATED BREECH DELIVERY

	Deliveries	Well	Stillborn	Dead	Macerated	Multiple births	Premature	Intracranial deaths	Mechanical deaths	Crude mortality %	Corrected mortality %
[illegible]	[illegible]	73		16		3	7		9	17	[illegible]
[illegible]	[illegible]	73		16	4			3	4	17	[illegible]
[illegible]	[illegible]	86	8	6					6	14	11.1
[illegible]	[illegible]	81	10	8	3		4		5	19	13.6
[illegible]	[illegible]	81	8	11			7	3		19	14
[illegible]	[illegible]	81		7	4		5		4	18	11.6
[illegible]	[illegible]	81	7			4	4			19	9.6
[illegible]	[illegible]	86	7	7	4				3	14	8.5
[illegible]	[illegible]	81	3	16			10		1	19	13.6
[illegible]	79	63	3	4		3			3	19	3.9
	[illegible]	[illegible]	39	[illegible]	18	16	38	16	32	18.5	13.8

TABLE XV —MORTALITY IN UNCOMPLICATED BREECH DELIVERY IN PRIMIPAROUS AND MULTIPAROUS, SINGLE AND MULTIPLE PREGNANCIES, FOR PREMATURE, IMMATURE, AND MATURE INFANTS

Primiparous Single Deliveries

	Cases	Well	Stillborn	Dead	Macerated	Multiple births	Premature	Intracranial deaths	Mechanical deaths	Crude mortality %	Corrected mortality %
Premature	43	8		24		4	10			84.3	18.7
Immature	41	32	5	5						17.7	10
Mature	313	286	3			5		3	17	8.6	6.3
	[illegible]	[illegible]	33	40	6			4	18	15	14

Multiparous Single Deliveries

Premature	13	11		10	8		17			64.3	1
Immature	33	30	3			3					
Mature	[illegible]	[illegible]	33	16	7	5		9	17	10.5	1
Unrecorded										100	
	447	379	40	37	17		17		19	17	11.4

Primiparous Multiple Deliveries

Premature	13	10		3			4			36	17
Immature	3	3									
Mature	7	7									
	23	18					4				17.4

Multiparous Multiple Deliveries

Premature	20			14						36.4	31.8
Immature	15	14									
Mature	33	29								9	6
	68	47		16						8	19

TABLE XVIII.—CRUDE AND CORRECTED MORTALITY IN UNCOMPLICATED BREECH DELIVERY (MATURE INFANTS)

	Deliveries	Well	Stillbirths	Dead	Macerated	Mal-formations	Premature	Intra-uterine deaths	Mechanical deaths	Crude mortality %	Corrected mortality %
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		[illegible]		[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]					[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]		[illegible]			[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]					[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]		[illegible]	[illegible]				[illegible]	
[illegible]	[illegible]		[illegible]						[illegible]	[illegible]	[illegible]
[illegible]	[illegible]		[illegible]						[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]			[illegible]	[illegible]	[illegible]

TABLE XIX.—CRUDE AND CORRECTED MORTALITY IN UNCOMPLICATED BREECH DELIVERY (MATURE INFANTS)

Primiparous Single Pregnancies

	Deliveries	Well	Stillbirths	Dead	Macerated	Mal-formations	Premature	Intra-uterine deaths	Mechanical deaths	Crude mortality %	Corrected mortality %
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]			[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]						[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]							[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]		[illegible]		[illegible]	[illegible]	[illegible]	[illegible]

TABLE XX.—CRUDE AND CORRECTED MORTALITY IN UNCOMPLICATED BREECH DELIVERY (MATURE INFANTS)

Multiparous Single Pregnancies

	Deliveries	Well	Stillbirths	Dead	Macerated	Mal-formations	Premature	Intra-uterine deaths	Mechanical deaths	Crude mortality %	Corrected mortality %
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]				[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]				[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]				[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		[illegible]	[illegible]	[illegible]	[illegible]

same finding and have accounted for it by stating that multiparae are more apt to give birth to large and overdeveloped infants. Our figures show that multiparous single pregnancies resulted in the birth of 42.4 per cent of mature infants weighing over 8 pounds, whereas of mature infants born of primiparae only 25.5 per cent occurred in the higher weight groups of 8 pounds and above. Of these however the corrected mortality among heavy first born babies proved to be 10.1 per cent while that among babies born of multiparae was 7.7 per cent. The factor of overdevelopment in this series, therefore did not account for the greater mortality in mature infants born by multiparous delivery.

Tables XVI and XVII show primiparous and multiparous single deliveries, respectively recorded when possible in blocks of 100, with the crude and corrected mortality in each block. Again, as in Table XIV the trend of mortality in recent years has been downward.

Crude and corrected mortality in immature and mature infants born by uncomplicated breech delivery. The final groups to be analyzed in this survey are the series of immature and mature infants born near or at term by uncomplicated breech delivery. The latter

the part of the mother and of hemorrhagic and other accidents of labor due to abnormalities of the placenta or of the umbilical cord

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ON THE DIFFERENT FORMS OF NON-GENERALIZED FIBROUS OSTEODYSTROPHY

The Localized, the Diffuse Monostotic, the Unilateral and the Monomelic Form

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THE question of localized (non-generalized) osteitis fibrosa is still very enigmatic despite the fact that during the last two decades a great number of investigators have tried to arrive at greater clearness From the pathologic-histological viewpoint the question is relatively simple in the more common cases, but a conclusive diagnosis is by far not always to be made merely on the basis of the microscopic study of a few slides The histological picture of osteitis fibrosa is a too frequent response of bone marrow to different damages and stimuli It may occur in a number of essentially different bony diseases, as inflammatory, neoplastic, metabolic, and simple mechanical disturbances, so that the histological diagnosis of osteitis fibrosa quite often may in the special case be more obscuring than clearing up It may at least hide as much as it reveals In a great number of cases it is only a symptomatic but not a nosological diagnosis

Nevertheless, there is no doubt that a great deal was done by investigation of pathology, and the recognition of localized osteitis fibrosa in all its forms as an essentially benign lesion signifies a great accomplishment This seems to be especially true for the giant cell tumors or brown tumors which nowadays are considered by the greater number of pathologists as granulomas rather than real neoplasms According to Lubarsch and many others, they develop following extensive hemorrhage in the bone marrow The resorption and organization of the hematoma occur with development of non-specific granulation tissue, which may assume tumor-like appearance Similarly, the cystic forms of osteitis fibrosa have been explained also on the basis of an extensive hemorrhage in the bone marrow, leading to increased pressure within the marrow spaces and impairment of the blood circulation, especially of the venous flow, von Recklinghausen's stage of phlegmasia, again newly introduced by Pommer as an important factor in bone pathology Bone tissue yields to this augmentation of pressure with osteoclastic resorption, and, by hydropic degeneration of the fibrous bone marrow, bone cysts may develop

Clinical observations seem to speak in favor of the just mentioned interpretation because of the relatively frequent observation of spontaneous healing of bone cysts and because of the good response to surgery and X-ray treatment Thus, we quite often find the topic of localized osteitis fibrosa treated in textbooks of surgery with great confidence and optimism as far as treatment and prognosis are concerned Nevertheless, every surgeon of some experience with cases of localized osteitis fibrosa knows that such cases do not always do as well as one would expect from the textbook descriptions Local recurrences are quite frequent and functional impairment of the affected extremity is by no means rare This is especially true for the group of giant cell tumors, which in many respects act quite differently from simple cases of osteitis fibrosa

For this discrepancy between textbook optimism and greater reservation in practice we thought it worth while to look over the material of localized osteitis fibrosa as it came to observation in the Surgical and Orthopedic Departments of the State University of Iowa

We do not intend to give here a detailed study of the pathological findings, although a good number of the cases presented have come to histological examination Neither can it be of greater interest to discuss more extensively the X-ray findings This has already been done too frequently and a good number of excellent articles are available Our main task is the classification of the different lesions It was planned to present the entire material in one paper, for external reasons, however, the giant cell tumors will be reported separately

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November 9, 933 June 8, 1934 October 8, 934

Fig. Case 2 Boy 8 years old Cystic lesion in upper metaphysis of humerus, with pathological fracture Improved by surgical treatment

We have divided our material of 25 cases into 4 groups.

A. Cystic and solid localized lesions of osteitis fibrosa, 18 cases

B Multiple localized lesions, 2 cases.

C. *Diffuse monostotic lesions*, 2 cases

D Osteodystrophia fibrosa unilateralis 3 cases.

GROUP A CYSTIC AND SOLID LOCALIZED LESIONS OF OSTEITIS FIBROSA

In group A the cystic and solid localized *lesions of osteitis fibrosa, there were 18 cases*, 9 males, 9 females The ages ranged from 2½ to 42 years the average being 11 1 years.

	Cases
First decade of life	3
Second decade of life	
Third decade of life	
Fourth decade of life	0
Fifth decade of life	1

CASUISTICS ACCORDING TO LOCALIZATION

Upper Metaphysis of the Humerus—4 Cases

CASE 1 Sixteen year old boy who 3 weeks before admission, while playing ball, felt a snap in the right shoulder and could not use his arm after that X ray pictures showed a cystic destructive lesion in the upper metaphysis of the humerus and a pathological fracture with good callus formation No follow-up

CASE 2 Eight year old boy fell 4 months before admission and complained of some pain in the right arm, which cleared *up soon Three weeks before* admission he slipped and fell forward on his arm There was a sudden moderate pain with disability X ray pictures showed a big cystic area on the upper metaphysis of the humerus the cortex was broken through in one place and reinforced by periosteal bone signs of a healing pathological fracture At operation the cyst in the humerus was found filled with brownish gelatinous material of the appearance of an older blood clot The cyst wall was formed by a layer of granulation tissue varying in thickness Careful curetting was carried out, the wound sterilized with 95 per cent phenol, and vaseline strips and shoulder spica were applied

One year after operation there was free motion in the shoulder joint and strength in the right arm is coming back. Patient was clinically improved X-ray pictures at three different occasions showed that after curetting, the cyst gradually became smaller the cortex became stronger but there still remained a very big cavity and it seemed doubtful whether it would ever fill in entirely

CASE 3 Eleven year old boy had quick bony consolidation after fracture of the right humerus 2½ years before admission T o years previously he fell and fractured the right humerus X-ray pictures showed a multilocular cystic lesion in the upper *metaphysis of the right humerus with widening of* the shaft and thinning of the cortex from within Patient was submitted to X ray treatment (five series within 1 year) The roentgenograms taken at different stages of the X-ray treatment show gradual improvement with better calcification the cystic areas are filling in and the cortex is becoming stronger the shaft is getting more and more straight

CASE 4 A boy 7 years old had a fracture of the *left humerus 15 months before admission—a slight* injury Fracture was reduced and immobilized for 6 weeks Healing was good The day of admission patient fell again on his shoulder and re fractured the humerus.

Patient brought the roentgenograms taken at time of first injury which showed a typical picture of a sharply outlined cystic area in the upper metaphysis of the humerus and a recent transverse fracture through the cystic area. Nine months later the cyst had increased to the length of 2½ inches There was good union of the original fracture and beginning organization of the cyst by bony trabeculation

At time of admission a fresh subperiosteal fracture could be seen running through the cystic area, with lateral angulation of the fragments Patient is immobilized in shoulder spica One year later excellent healing with good correction of the deformity was present The cystic area had entirely disappeared, and there was only very slight irregularity of the bony structure

Case of bone cyst in the upper end of the humerus *with two pathological fractures* Treatment was by immobilization The first fracture was followed by increase in size of the cyst the second by excellent healing

Upper Metaphysis of the Femur—8 Cases

CASE 5 Twenty-six year old woman For 4 years dull and aching pain was noted in left hip, as well as muscle spasm X-ray pictures showed a cyst in the region of the greater trochanter *well outlined* and of the size of a 25 cent piece Hip as in

March 10, 1934 July 20, 1934 October 12, 1934 February 1, 1935

Fig. 2. Case 3. Boy, 11 years old. Cystic lesion of upper metaphysis of humerus, with considerable improvement under X-ray therapy.

mobilized in a plaster cast. Four months later the cyst was filling in; 2 years later the roentgenograms revealed normal conditions, with no cystic area.

CASE 6. An 11-year old boy had limp and pain in the right groin for 9 months. The X-ray picture showed a cyst in the neck and the upper end of the shaft with incomplete fracture. The parents refused to have the child operated upon and a hip spica cast was applied. Seven years later patient was feeling all right. He had no pain, hip motion was limited and there was some limp. No roentgenological check up was made.

CASE 7. A 21-year old girl had limped for 1 month following a fall. The X-ray picture showed a cystic area occupying almost the entire neck of the femur with some periosteal bone production, especially on the outside of the metaphysis. A long hip spica cast was applied. Six months later the cyst had enlarged and the bone was definitely blown up. There was no break in the cortex. One year later (7 years after injury), good healing had taken place with better calcification and a coarse system of new bony trabeculæ.

March 8, 1934 April 17, 1935

Fig. 3. Case 4. Boy, 7 years old. Pathological fracture through cystic lesion in upper metaphysis of humerus. Good healing under conservative treatment.

CASE 8. A 10-year old girl had a fracture of the upper third of the femur, at which site she had had a fracture before. X-ray pictures showed a big cystic area in the upper end of the diaphysis with pathological fracture and marked varus deformity. There was inward displacement of a piece of the inner cortex. The cortical bone on the outer side was very thin. A double hip spica cast was applied. X-ray pictures, 3 months later, showed good bony healing with filling in of the cavity and a good deal of the deformity corrected. One year later patient started to limp again. Roentgenograms revealed slipped epiphysis.

CASE 9. A woman 28 years of age, 5 months before admission, while doing ordinary housework, began to limp. Motion in hip and knee was quite painful. Immobilization in cast and bed rest were maintained for 5 weeks. X-ray pictures at admission showed a very extensive destructive lesion in the upper end of the femur with extension into the head. There was a pathological fracture through the neck with marked coxa vara deformity. The cortex was thinned, but was not broken through. There was no periosteal bone formation. A hip spica cast was applied. Roentgenograms 1 year later showed good bony union at the site of the fracture. There was better calcification in the cystic area.

September 17, 1927 February, 1928 February, 1929

Fig. 4. Case 7. Girl, 2½ years old. Cystic lesion in upper metaphysis of femur. Good healing under conservative treatment.

April 3, 931 October 30, 93

Fig 5 Case 3 Man, 44 years old Cystic lesion in upper metaphysis of tibia, following trauma Pathological fracture following curettage

Case 10 A 12 year old boy had a fracture of the right femur 3 months before admission to the hospital. Six years previously he had had a fracture at the same site which healed perfectly Roentgenograms showed a large multilocular cystic lesion in the upper third of the femoral shaft, with marked varus deformity A subtrochanteric osteotomy was performed to correct the varus deformity Six months later good alinement was present with increased density of the cystic area as a sign of healing tendency

Case 11 A 5 year old boy had had a limp and slight limitation of motion in the right hip for the last 3 weeks. Roentgenograms showed a big cyst in the upper end of the femur 1 to 1¼ inches in diameter At operation, a large cyst of the size of a hen's egg was opened below the greater trochanter, scraped, and cleansed with tincture of iodine and alcohol. A plaster cast was applied Recovery was uneventful Patient was seen again 5 years later when he had no shortening, no limitation of motion—clinically perfect result. No X-ray check-up was made

Case 12. A 6 year old boy had had a limp for 1 month Roentgenograms showed a 3 inch long cystic lesion in the middle and lower part of the neck of the femur No pathological fracture was noted At operation, the cyst was opened The walls were covered by soft granulation tissue which was carefully scraped out An iodoform drain was inserted and a cast applied Roentgenograms, 6 months later showed good healing, the cavity being almost filled in No further follow up has been made

Upper End of the Tibia—2 Cases

Case 13 Patient aged 44 years, male, 18 months before admission received a severe blow over the upper end of the tibia from a pack ax The skin was broken but the bone was not exposed The wound healed quickly but quite marked pain in this region persisted Weight loss was 30 pounds Roentgenograms showed an extensive destructive lesion, purely osteoclastic, involving the upper end of the tibia with destruction of the anterior cortex There was practically no periosteal bone production

At operation, a cavity was found in the upper end of the tibia, filled with rather tough grayish kite tissue, which could easily be peeled from the adjacent normal bone. Thorough curetting was done and a plaster cast was applied Pathological report osteitis fibrosa.

Following operation, patient was able to walk, but with some difficulty and pain persisted He gained 30 pounds Six months later he fell and fractured the leg at the site of the cystic lesion X ray pictures revealed further extension of the lesion and a fine transverse fracture line Patient insisted upon amputation, which was performed

Case 14 An 8 year old girl had some pain and limp of right leg, following direct trauma to the right tibia 2 months ago. Roentgenograms a short time after the injury showed a small fracture, and 1 month later a cystic lesion in the upper end of the tibia at the site of previous fracture. Roentgenograms at admission showed a slightly lobulated cystic area in the upper metaphysis of the tibia surrounded by some sclerosed bone tissue Periosteal bone production (callus formation) was also noted

At operation, the bone cyst was found filled with a yellowish-brown cellular matrix The area was thoroughly curetted, 95 per cent phenol, alcohol, and iodine used, and a plaster splint applied Brodie's abscess, which had to be considered especially from the roentgenological viewpoint, could be ruled out by histological and bacteriological examination

Lower End of the Tibia—1 Case

Case 15 A 17 year old boy 03 years previously had had a severe trauma to the left foot and could not walk for 2 months During the following 2 years walking was very much impaired, and there were some draining sinuses Six months ago he twisted his foot, and immediately after he could not walk The ankle was swollen and painful Bed rest is maintained for 2 weeks Roentgenograms showed a clear cystic area of the size of a goose egg, with ex

April 20 1935 July 12 1935 September 1, 1934

Fig 6 Case 15 Boy, 12 years old Cystic lesion in lower metaphysis of tibia treated by curettage and bone chips Good healing with obliteration of the cyst

pansion of the bone and thinning of the cortex in the lower metaphysis of the tibia Practically no periosteal reaction followed The lower epiphyseal plate was well preserved

At operation, the periosteum was found to be thickened and edematous The cortex was very thin, the cyst was filled with serosanguineous fluid and was well outlined with a soft edematous membrane A thorough curetting was done and bone chips from the tibia were filled in the cavity A plaster cast was applied The following month the wound was opened at several places and some of the bone chips became sequestrated The patient was seen again 18 months after the operation when he had no complaints, the wound was dry, the ankle free, and he had no tenderness The lower end of the tibia was getting decidedly smaller and the defect was filling in very nicely

Diaphyseal Lesion—3 Cases

CASE 16 A 14 year old girl 8 years, 5 years, and 1 year previous to admission had had fractures through the diaphysis of the left humerus The fractures healed well Roentgenograms showed a typical cystic lesion in the middle of the diaphysis Four years later the patient stated that the swelling reappeared in the arm with some aching pain No X-ray check-up was made

CASE 17 A 10 year old girl suffered trauma to the right tibia 6 years prior to admission She had 2 weeks of bedrest There was no limp, no pain Three years later she bumped her leg in the same place and a very painful swelling appeared Swelling never went down to the original size but seemed to increase after each occasional trauma On physical examination, a spindle shaped mass at the junction of the middle and upper thirds of the right tibia was seen, with discoloration of the skin, and tenderness She was unable to walk because of pain

The periosteum was stripped off and a granulated, soft, yellow tissue was encountered, with numerous cysts Thorough curetting of cavity (4 to 2½ inches) was done There were no areas of fracture of the tibia Long leg cast applied, then a brace

Roentgenograms 6 months after operation showed at the junction of the upper and middle thirds a multilocular cystic area, involving the anterior cortex, leading to thinning out of the cortical bone, and blowing up of the diaphysis There was marked anterior bowing of the tibia at the site of cyst, but no breaking through of the cortex No further follow up was made

CASE 18 A girl 2½ years of age, had injured the tibia 6 months and 1 month previously Fracture was of the greenstick variety Plaster cast was applied The leg gradually became weaker and swelling increased Roentgenograms 1 year after the first injury showed marked thickening of the middle of the tibial diaphysis The diaphysis was interrupted for about 1 inch by a cystic porotic area Only a thin shelf of bony tissue extended along the outer surface of the cortex as periosteal bone The soft tissue showed no involvement

After removal of the eggshell like cortex the bony cavity was found to be filled in by solid homogenous tissue, which was entirely curetted out The wound was then treated with 05 per cent alcohol, Dakin's solution, and vaseline strip Following operation the patient walked with a limp Four months later the bony swelling began to return and a second operation was performed A radical curettage with removal of all tissue filling the bony cavity Ninety-five per cent carbolic acid was applied Resection of all diseased bone was considered, but it seemed that local removal offered a fairly good chance

In all 3 cases of diaphysis lesion it appeared certain that the lesion started primarily in the diaphysis and not in the metaphysis This fact may be emphasized because one finds quite often the statement that diaphyseal cystic lesions are due to gradual displacement of a primary metaphyseal lesion toward the center of the diaphysis If such a displacement, due to the length growth of the bone by enchondral ossification, were an important

factor we would expect to find diaphyseal lesions more often

All the cases presented have been verified by histological examination as far as they came to operation. Cystic and solid forms were considered under the same group of localized osteitis fibrosa and this difference in *morphological appearance has been taken only* as one of degree. In quite a number of cases, a variable amount of giant cells was present in sections, but we did not think that their *irregular distribution* and *relative* scarceness compared with the fibrous tissue which dominated the picture would justify the term "giant cell tumor It is known, however that there may be fluent passages from osteitis fibrosa to giant cell tumor as far as the histological picture is concerned

An important question in cases of localized osteitis fibrosa is the significance of trauma. It is known how difficult it is to rule out definitely traumatic etiology in any skeletal lesion especially in childhood For a number of osteitis fibrosa cases, however trauma seems to have more than accidental importance At least from the clinical viewpoint, there is no doubt that a great number of cases come to clinical observation following trauma. Quite often however the trauma mentioned in the history is insignificant but it may lead easily to *infraction or complete fracture of the diseased area*. If roentgenograms are taken at this time, the fracture is evidently pathological It runs through a cystic area of the skeleton *The bone cysts must have developed* insidiously for some length of time previous to the fracture which led to the clinical recognition of the lesion The pathological fracture has *therefore, no etiological importance for* the development of the bone cyst It is a secondary complication and not a primary causative factor However there are quite a number of cases in which definite trauma preceded the occurrence of recognized pathological fracture for some time. In cases of repeated fractures at the same localization especially in which the roentgenograms at the time of first fracture did not reveal pathological condition of the broken bone, it is quite possible that the first fracture may have led to an extensive hematoma of the bone marrow the organization of which resulted in cyst formation.

In our series of 18 cases, pathological fracture *at time of admission to the hospital* was present in 11 (Cases 1 2 3 4 6 8 9, 10 13 16 18) Five out of these had 2 fractures at the same site (Cases 3 4, 8, 10, 18) and 1 (Case 16) even 3 but in 3 of these cases there is doubt whether the first fracture can be considered as pathological in the absence of definite X ray findings at that time The occurrence of the second fracture at the same site suggests however a causal connection which most likely is represented by the bone cysts developing after the first fracture Definite X-ray evidence that the cyst developed 1 month after fracture through the upper metaphysis of the tibia we find in Case 14 Severe trauma, although not leading to fracture, was also present in Cases 13 and 15 and we have reason to believe that in these cases trauma is of primary importance for the formation of a bone cyst.

The 8 cases which did not show definite signs of fracture at the time of admission were complaining of weakness, with limp if the lower extremity was involved. And, as a rule, the symptoms became manifest after a fall. Weakness of the affected bones, pathological fractures, and limp are, therefore, the most important among the early clinical symptoms of localized osteitis fibrosa. Pain, as a rule, is due to the pathological fracture and irritation of periosteum but not to the disease itself

The question arises as to the curative importance of the pathological fracture in bone cyst It is a frequent statement especially in the German literature that bone cysts heal *after pathological fracture*. The explanation given is that the fracture leads to decreased pressure within the cyst. This statement is based partly upon clinical observation partly *however upon the assumption* that bone cysts derive from bone resorption following increased intermedullary pressure caused by an extensive hematoma

In our group there are 7 cases with pathological fracture in which only conservative treatment was followed (Cases 1 4 6, 8 9 10 16) One (Case 1) is entirely without follow up in 5 instances (Cases 4 6 8 9 10) definite

February 21, 1930

Fig 7 Case 17 Girl 10 years old Multiloculated cystic lesion of tibia diaphysis involving the anterior cortex Anteroposterior and lateral views

October 6 1924

Fig 8 Case 18 Girl 2½ years old Diaphyseal lesion, involving the cortex Anteroposterior and lateral views

improvement could be noticed following the fracture with increased calcification of the diseased areas in the roentgenograms Case 4 especially showed perfect healing of the cyst cavity following the second pathological fracture One case (Case 16) with two refractures, showed good fracture healing But 4 years after the last fracture swelling reappeared and although roentgenograms were not taken the patient's description is very suggestive of an increase in size of the bone cyst So of 6 cases, apparently only 1 was not improved by the fracture, on the contrary it showed increase in size of the bone cyst It is true, however that the observation time of the 4 cases which showed improvement is relatively short Only 1 case (Case 6) is followed up for 7 years following first admission, in all the other cases the last control examination was around 1 year after the fracture Therefore we can conclude only that the occurrence of pathological fractures in bone cysts may lead to improvement and in some cases even to permanent cure, but we are, on the basis of our material, not able to give any definite statement as to how often a pathological fracture is followed by permanent healing of a bone cyst

The improvement following fracture can be explained by two factors the one already mentioned is a decreased pressure with its bone resorbing effect, the other is a stimulus to osteogenesis and callus formation, leading to better calcification and the appearance of coarse trabeculation in the roentgenograms

If this is true and if the pathological fracture in itself has a good influence upon the healing process of bone cysts then of course, we have to expect even more from surgical interference

Of 18 cases 8 were treated surgically, the procedure usually consisting in cutting a window in the thinned cortex and in scraping or curetting out the cavity as thoroughly as possible Then the cavity is swept out with 95 per cent phenol or iodine tincture and alcohol In 1 patient (Case 15) bone chips were used from the same bone (tibia) to stimulate bone formation Two cases have to be ruled out because of lack of control examination following operation One patient (Case 11) made a good and lasting recovery (5 year observation) following scraping of a cyst in the upper end of the femur In another case (Case 12), in which the cyst wall was likewise scraped, the

cavity was almost *entirely* filled by bone tissue 7 months following operation. In Case 2 with 1 year of observation there are some signs of improvement but the cavity is still very big and does not show a more marked tendency of getting smaller

Very definite is the improvement in Case 15 in which after the scraping of the big cyst in the lower end of the tibia, a good *number of* bone chips were used to fill the cavity In this case, 18 months after operation there was such marked improvement, clinically and roentgenologically that permanent cure can safely be expected. The sequestration of a number of bone chips a short time after operation did not interfere with the result.

There remain 2 cases (Cases 13 and 18) with decidedly poor results. In Case 13 patient sustained a pathological fracture following curettage of the cystic area in the upper end of the tibia which 6 months after the operation, did not show any healing tendency Patient insisted upon amputation. The other case a diaphyseal cyst of the tibia in a young child of 2½ years, showed progression despite the occurrence of a pathological fracture. The radical curettage was followed by recurrence within 2 months. *A second thorough curettage* was performed, but the child did not return to the clinic for further check-up

Of the 6 cases treated surgically 4 showed improvement (observation tim varied from 7 months to 5 years following operation) 1 patient (Case 2) 1 year observation, showed clinical improvement but the roentgenograms *still revealed a big cystic area. Two cases* (Cases 13 18) had to be considered failures.

In Case 18 It is true, we do not know how the second operation came out. The first one however was very rapidly followed by recurrence This case we think, has certainly a *tendency to local malignancy* It seems to belong to a certain group of cases in which the bone cyst is filled with solid tissue It is, therefore, not a real, but a pseudo cyst. This group can best be termed "borderline cases *to malignancy* They are more *frequently* observed with giant cell tumors We shall discuss this group later more in detail

Somewhat different is Case 13 In this man of 44 years, it is very likely that the severe trauma to the upper end of the tibia resulted in traumatic necrosis of the bone, followed by bone resorption and cyst-like appearance The thorough curettage weakened the bone even more and so there is no wonder that a fracture occurred in the weakened *weight bearing bone.* The leg was amputated despite the fact that there were no definite signs of local recurrence or more marked extension. Decisive was the patient a desire to get back to work as quickly as possible

The good result obtained in Case 15, in which a large cyst showed very fast and good healing after curettage and grafting of bone chips, the very slow healing in Case 2 and the failure in Case 13 suggest very strongly that *the filling of the scraped cavity with transplanted* bone is the treatment of choice Especially in greater cavities and in older individuals in whom the power of osteogenesis has become lowered it seems that we cannot expect a complete bony obliteration of the cystic defect by spontaneous bone production. This seems, as we shall see, to be even more so in the group of giant cell tumors.

In 1 case (Case 3) instead of surgery X-ray treatment was followed Very definite improvement *could be seen within 1 year* Although there is a pathological fracture in the history it seems that the healing process has entirely to be attributed to the irradiation because 4 months elapsed *without improvement* between fracture and first X ray treatment. One case is, of course, not enough to draw any conclusions, but it seems that X-ray *treatment* can be used quite advantageously in a number of cases of bone cysts.

Finally 2 cases have to be mentioned (Cases 1 and 3) *in which healing* occurred without any manifest pathological fractures or any special treatment besides immobilization in plaster casts One case (Case 3) 1 3 years after admission to the clinic showed good filling in of the bone cysts the other 2½ years after admission, does not reveal any pathological structure in the roentgenograms These 2 cases prove that spontaneous healing of bone cysts is possible with *restitutio ad integrum* of the bony structure but it is certainly rare. It can *however not* be ruled out that some *small fractures* which could not be rec

ognized roentgenologically were present in these cases.

The 18 cases presented were typical inasmuch as they showed a localized lesion of the skeleton in the sense of cystic or solid fibrous osteitis. In quite a number of these cases the X-ray pictures of other portions of the skeleton were taken but did not reveal any pathology. We found, however, in our material 6 cases which do not fit entirely into the group of localized osteitis fibrosa or belong to the generalized form. From a study of the literature, it does not seem possible that a true case of localized osteitis fibrosa ever changes to a generalized form in the sense of von Recklinghausen. There is one case reported by Bergmann, a case of localized osteitis fibrosa when at the age of 8 years healed well. Thirteen years later, however, the patient developed besides a local recurrence a typical picture of generalized fibrocystic disease.[1] It seems to me, however, that this is only by coincidence and there is no proof that the generalized form developed from the localized one. From the following cases, it will appear that between the monosteotic sharply localized cases and the generalized forms with all the characteristic changes in calcium metabolism, we have cases with several similar lesions in the skeleton, each of them well localized, then cases in which one bone of the skeleton is extensively involved and finally, cases with a strictly unilateral distribution following certain anatomical structures. However, all of these cases with more extensive involvement of the skeleton do not represent stages of passage to the generalized form. They are typical of the normal blood chemistry and there is nothing to suggest an endocrine disorder.

GROUP F. MULTIPLE LOCALIZED LESIONS

CASE 19. A girl, 12 years of age, had a stabbing pain in the right arm for last 10 months. The roentgenograms showed a multilocular cystic lesion in the lower half of the right humerus with thinning of the cortex and blowing up of the shaft.

At operation, the bone cavities were found filled with solid parts of granulated material and some cystic areas were present. The area was curetted. Two heavy tibial bone grafts were used to fill the defect. X-ray picture following operation showed a heavy inlay medullary graft, but the cavity was not filled completely. A picture of the tibia from the area from which the bone graft was removed showed good regeneration 2 months following operation. An incidental finding was a small cystic area in the lower epiphysis of the tibia involving the inner cortex. This cavity was in relation to the bone defect.

Six months after the first operation, the cystic area of the tibia was exposed. The cyst was well curetted and bone filled in. X-ray pictures taken 1 year after the first operation showed the bone graft well incorporated into the bone. The cystic lesion was well healed but not healed. There were no signs of recurrence present. The cystic lesion in the lower end of the tibia was still present.

X-ray pictures taken at different occasions from 6 to 8 years after first operation always showed the cystic lesion. Medullary bone in the femur and tibia seemed to be intact. Pictures of all bones of the skeleton were taken and only a small cyst was found in the inner cortex of the left femur at the junction of the middle and lower third. Clinically, the patient felt the only slight discomfort and pain in the right knee. The blood chemistry revealed normal value.

CASE 20. A patient, a girl, 11 years old, had a slight injury to the right leg in the last 6 months. Patient fell the day before admission and hurt her right leg. All pertinent anamnestic data of symptoms. Roentgenograms showed to a considerable extent an irregular cystic lesion in the middle and lower third of the tibia and a little lower of the tibia an irregular cystic area with periosteal reaction and reactive bone production around the cystic areas. Similar changes were also present in the upper third of the tibia, especially where the inner posterior cortex was involved. There was anterior and valgus bowing of the tibia.

Patient was given a short leg cast. She returned 2 months later. Laboratory work was essentially negative, tuberculin test, Wassermann reaction and blood chemistry. Biopsy from tibia showed osteitis fibrosa.

The valgus bowing of the tibia rapidly became worse under the weight bearing stress despite the brace. The leg was therefore manipulated under anesthesia and a long leg cast was applied. Roentgenograms 6 months after first admission showed that the lesion had progressed in the lower part of the tibia where a definite cystic area with increased valgus deformity could be seen following pathological greenstick fracture. At the site of this pathological fracture between middle and lower thirds of tibia a definite pseudarthrosis developed. Considerable periosteal reaction was present, probably due to the fracture (callus formation).

Operation was done 10 months after first admission. Exploration of the site of the deformity revealed pseudarthrosis with fibrocartilaginous tissue interposed between the bony ends. Beck's drilling,

[1] Bergmann, E. Moeller: Klinische Beiträge zur Chirurgie, Band 1, Heft 1, 1907.

April 927 October 5 1927 June 17 1929 August 3, 1932

Fig 9 Case 9 Girl, 3 years old Multiloculated cystic lesion in lower half of humeral diaphysis. Good healing following curettage and bone graft

July 18, 927 August 5, 03 January 7 930

Fig 0 Same case, showing circumscribed cystic lesion in the outer cortex of the tibia from which the bone graft has been removed ( ) f Same lesion after curettage g. Accidental finding of cortical cystic lesion in femur

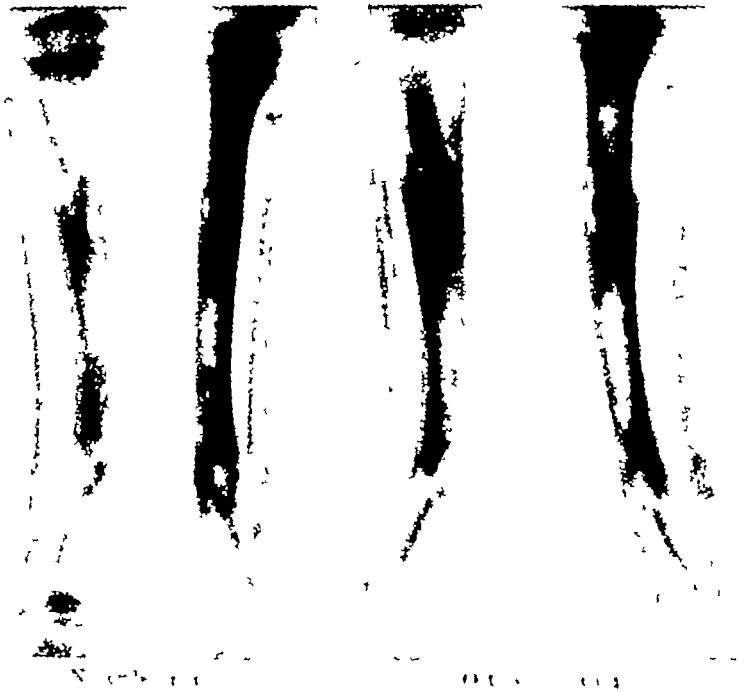
correction of deformity A cast was applied and later was changed to brace

Patient was seen at several occasions She ailed with a limp but without pain She had no complaints except an increase of the valgus deformity of the right leg which is definitely longer than the left Extensive curettage with massive bone graft from the other tibia was considered

Some of the roentgenograms in the last case were somewhat suggestive of a connection between the two lesions in the tibia in the sense that there was not a double lesion separated by normal bony tissue but only one extending almost through the entire diaphysis Without doubt such an extensive bony involvement was present in the two following cases which, at first impression seemed to be simple cases of localized osteitis fibrosa The findings, at time of operation however and the slowly but constantly progressive character of the lesion leading to an extensive invasion of the marrow cavity pointed toward a separate position among the cases of osteitis fibrosa

GROUP C. OSTEITIS FIBROSA DIFFUSA MONOSTOTICA

CASE 21 A girl, aged 1 years, complained of an increasing limp during the last year The limp started following trauma to the right hip when she



[illegible]

[illegible] Roentgenograms showed a large [illegible] the [illegible] of the shaft of the femur with irregular mottled structure of the bone [illegible] upon most probably [illegible] in the [illegible] The proximal [illegible] of the lesion [illegible] sharply [illegible] gradually blended into the normal [illegible] The proximal end of the shaft [illegible] enlarged the outer cortex was thinned [illegible] and [illegible] The [illegible] showed no bending of the femur Blood chemistry examination and other laboratory tests were negative

At operation, the cortex in the trochanteric area was opened and a small amount of serous fluid escaped The content of the cavity consisted of blood clot fibrous tissue with calcium deposit The cavity was curetted and filled with thin tibial bone grafts A hip spica was applied Bacteriological tests were negative Pathology report osteitis fibrosa

Six months after the operation the bone grafts were resorbed to a great extent and did not lead to more marked osteogenesis The lesion in the upper end of the femur had extended downward and occupied almost the entire upper third of the shaft There was another area of more circumscribed osteoporosis at the junction of middle and lower thirds Three months later, the roentgenograms were essentially the same, but there was another area of porosis with irregular calcification a little below the first described lesion The lateral cortex was considerably thinned out Sixteen months following operation the roentgenogram showed some increased calcification at the site at which the bone grafts were put in The irregular structure in the femoral diaphysis was no more evident especially the cortical focus at the junction of middle and lower thirds was quite sharply outlined and defined by some osteosclerosis All other bones of the body were negative Six months later (2 years after operation) there was no doubt about the very extensive involvement of the femoral diaphysis and especially of the outer cortex which was very thin by erosion from within (eccentric atrophy) The process extended from the upper metaphysis downward to the junction of middle and lower thirds It led to marked osteoporosis and irregular bony structure but without definite cystformation Varus deformity of shaft and neck

Patient had been well all the time, she walked with the typical gait of a coxa vara At times after walking a long way she had some pain at the upper end of the femur Inasmuch as the X ray pictures showed a very slow but definite progress of the lesion and deformity another attempt at curettage bone grafting and corrective osteotomy seemed to be indicated

Second operation (2 years after the first) Through a longitudinal lateral incision, the upper half of the right femur was exposed from the trochanter down

August 16, 934 January 935.

Fig 3 Case 1. Girl, 9 years old Extensive cystic lesion in upper end of femur treated by curettage, bone grafts, and, finally oblique osteotomy through the diaphysis of the femur to correct the varus bending

ward The periosteum was stripped, the cortical bone was found atrophic but smooth There was considerable thickening of the periosteum over the trochanter There was also a small defect in the bone, filled by scar tissue, at the site where a *window* was cut in the bone at time of first operation The whole upper end of the femur and the medullary cavity were filled with a firm, white tissue of rather high consistency in which a few specules of bony tissue were included Only in the region of the greater trochanter some grayish white and soft granulation tissue was encountered. The tissue was expanding toward the cortical bone which showed roughness by erosion on its inner side At time of operation it seemed that the entire pathological tissue was removed from the upper half of the diaphysis Normal bony marrow was encountered at the distal end of the saucerization To judge from the roentgenograms, however, some foci in the lower half of the diaphysis remained It did not seem wise to correct the deformity of the femur by an osteotomy *at the same time The bone was quite porotic* and even more weakened by the radical operative procedure A hip spica cast was applied

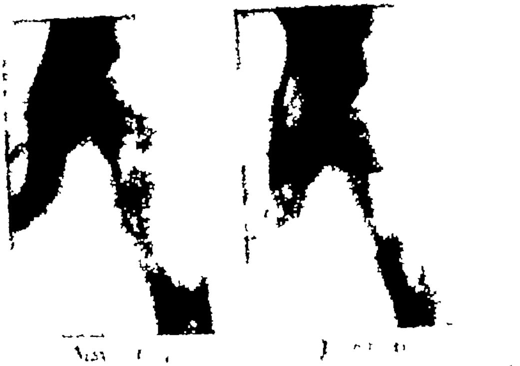
Pathological examination of the removed tissue showed very dense fibrous tissue with relatively few vessels Bony trabeculæ were imbedded in an irregular way Most of them were of fibrous type with good calcification of the central portion, whereas the superficial layers were still osteoid Wherever bony trabeculæ appeared, the bone marrow in their neighborhood was loose rich in cells and vessels, and stood out very distinctly by its paler stain from the surrounding dense fibrous marrow It was frequently found that smaller foci of younger and therefore looser bone marrow were almost completely surrounded by a group of bony trabeculæ In these places the outer side of the bony trabeculæ was rather smooth and the dense fibrous bone marrow showed concentric condensation of its fibers parallel to the bony trabeculæ The inner surface which faced the loose bone marrow was more irregular, sometimes showing osteoblastic bone apposition, sometimes osteoclastic bone resorption The cortical bone had undergone marked *resorptive changes* from the endosteal surface Fibrous bone marrow was invading the cortical bone along the haversian canals There was very little periosteal reaction on the outside. The picture was that of a more advanced stage of osteitis fibrosa with extensive scarring of the fibrous bone marrow In some places the scar formation reached such a degree that large areas were seen without any bony tissue and with beginning hyaline degeneration of collagenous fibers

Patient made an uneventful recovery Three months later to correct the marked varus deformity of the neck and shaft, a long oblique osteotomy was performed A defect in the cortex still remained *The medullary cavity was found to be filled with the* same dense material as at the time of first operation recurrence of osteitis fibrosa. The bone was curetted out thoroughly The distal fragment of the femur was brought into abduction to correct the varus deformity A cortical bone graft was removed from the same tibia and placed in the cavity in the trochanteric region. A double hip spica cast was applied.

X ray pictures showed very good correction of the deformity following oblique osteotomy The cast was removed 3 months after operation The osteotomy was solidly healed and weight bearing was allowed in a short hip spica cast, and 8 months after operation without any support. There was no pain, but there was still a marked limp due to the abductor insufficiency (coxa vara) X ray pictures 10 months following osteotomy showed perfect healing of the osteotomy with very good callus formation. The upper two-thirds of the femur showed a great number of small cystic areas with a coarse system of *trabeculæ between them and very good calcification* Still, from the X-ray pictures, the process seemed to be active

Before entering the discussion of this unusual and interesting case of osteitis fibrosa we shall report another case which in many respects is similar to Case 21

Case 22 A male, 13 years of age, when 12 years old had a sudden sharp pain in the middle of the shaft of the left femur with muscle spasm Such an attack of pain recurred frequently especially when walking to school (2 miles) *Three weeks after the* initial episode he slipped and fractured the left femur He was put in traction and cast. At the age of 16 the same type of aching recurred X-ray pictures were taken and *showed cavities in the bone*, and the doctor told him that the fracture had been path-



[illegible]

[illegible]

[illegible] February 11, 1932

Fig. [illegible]

[illegible] He used crutches for [illegible] [illegible] the left leg was [illegible] [illegible] [illegible] [illegible] treatment being [illegible] and at times [illegible] [illegible] pain in the left [illegible] [illegible]

[illegible] of the left [illegible] [illegible] the middle [illegible] [illegible] fracture [illegible] [illegible] [illegible] phosphatase [illegible]

X-ray pictures [illegible] cystic [illegible] in the upper end of the shaft of the left femur extending into the neck of the femur and farther down into the diaphysis. The lower end of the lesion [illegible] [illegible] in the pattern [illegible] not sharply outlined.

At operation the cortex of the upper end of the femur was [illegible] Under the cortex, very dense white fibrous tissue was encountered. There was no real cyst formation. The fibrous tissue extended proximally into the neck of the femur, distally it extended beyond the level at which exposure was made. The bone over the cortex did not seem to be involved. Only the medullary cavity was filled with fibrous tissue. This tissue was cleaned out thoroughly with a curette but no attempt was made to follow the process up into the neck, and distally the operative procedure stopped at the point at which the fibrous tissue narrowed down into the medullary cavity. A heavy tibial cortical bone graft was cut in several pieces and jammed firmly into the cavity of the femur. Immobilization in plaster splint. Patient made a good recovery.

X-ray pictures 1 month after operation showed the window in the lateral cortex of the subtrochanteric region. The cavity had been filled with a number of heavy cortical bone grafts. The femoral diaphysis showed widening of the shaft with several cystic areas, quite of the same appearance as in the upper third. Most marked widening, spindle shaped and [illegible] cortex was present in the middle of the diaphysis, where the bone was blown up and the cortex thinned down to a paper-like shell on one side, where as the other showed definite periosteal bone apposition. Through this area ran an irregular transverse line suggestive of the old fracture which had healed through good bony callus formation. The bony structure was very irregular mainly consisting of osteoporosis with clouding and thinning of the cortex from within (eccentric bony atrophy). The pathological change extended almost continuously from the upper third down to the junction of the middle and lower thirds. There was no soft tissue involvement.

Patient returned 2 years after the operation stating that after leaving the hospital he gradually began to use the left lower extremity. Five months ago, however, the original symptoms reappeared in the same intensity so that he had to use crutches again. Blood chemistry at eleven different occasions showed normal values. On the basis of the X-ray pictures, however, the remote possibility of being a case of hyperparathyroidism was considered. X-ray pictures of all the bones of the body were taken but were negative with the exception of the left femur. An exploratory operation of the parathyroid glands was performed. All four glands were exposed, but there was no evidence of enlargement in any. None of the glands was removed.

Patient was seen last 3½ years after operation. He had been walking off and on with crutches. He

Fig 14 Case 21

Fig 14 Case 3 Girl, 3 years old Unilateral lesion of fibrous osteodystrophy Anteroposterior view of the left humerus Anteroposterior and lateral views of fore arm, showing the involvement of the radius and bones of the thumb Anteroposterior view of left femur with marked cortical

had no complaints At follow-up examination the X ray pictures showed essentially the same condition The bone grafts had taken well and it seemed that the upper portion of the porotic area was filling in nicely but the porotic changes in the diaphysis were still the same

Both cases (Cases 21 and 22) have in common the fact that an apparently simple case of osteitis fibrosa—as far as one can judge from the X ray pictures taken at onset of clinical symptoms—does not show a tendency to heal but rather a slow but definite, progression with gradual involvement of the upper two-thirds of the femoral diaphysis. The process remains, however confined to one bone and there is no soft tissue involvement It is a question whether the lesion extends simply through continuity or whether there are several foci separated from each other by normal bony tissue and bone marrow The roentgenograms in Case 21 would suggest the latter possibility and so would also the findings at the time of operation, when the lower end of the lesion was reached in the marrow cavity without touching the definite X ray focus in the lower third From the study of the histological sections one has to admit, however that the spreading of the lesion may follow the vessel canals of the haversian systems in the cortical bone besides the bone marrow spaces and so roentgenologically apparently isolated medullary foci may still be coherent with the main focus.

Both cases show practically no real cyst formation The bony cystic areas are filled with dense white fibrous tissue of relatively high consistency The density of the fibrous tissue seems to be a characteristic sign of these lesions It cannot be considered as a simple form of scarring due to the long duration of the process because the same material had reformed in Case 21 during the 4 months which elapsed between the second and third operations It is questionable, however whether the described histological changes with the peculiar interposition of loose fibrous bone marrow in dense almost scar-like fibrous tissue warrants a separation of these cases from other cases of osteitis fibrosa, also from the histological viewpoint. Further pathological study is necessary here to decide this question

With the tendency to expansion goes also a certain resistance to surgical procedures Case 21 was operated upon three times and still showed roentgenographic signs of activity The same is true with Case 22 in which the

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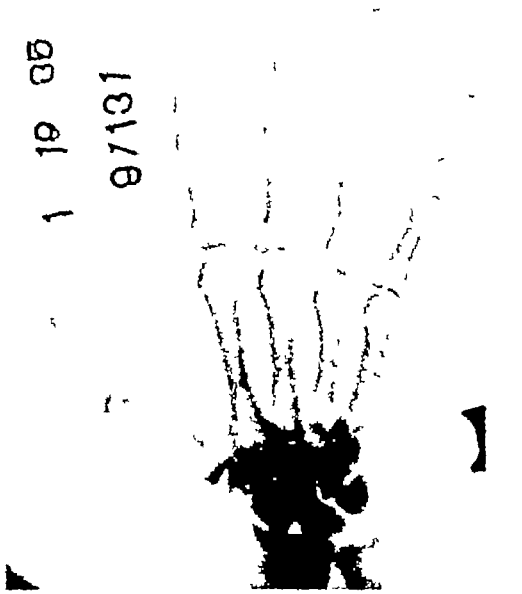

[illegible]

nb oeystic process could not be stopped by an extensive curettage and bone graft operation It is true that despite the most thorough removal of the pathological tissue in none of the cases of osteitis fibrosa can one be sure that all tissue has been removed However this does not seem to be necessary as many cases responded well to the routine surgical treatment Osteitis fibrosa is not a neoplastic but a dystrophic disease of the bony tissue and the cleaning out of the diseased tissue aims more at stimulation and making room for new and normal bone growth than at radicality in the sense of surgical attack of a tumor But this is what for some unknown reason this type of case of osteitis fibrosa lacks the endosteal bone production in a very extensive portion of the diaphysis does not lead to normal bone but to dense fibrous tissue with a few bony trabecula or primitive fibrous bone tissue The periosteal bone formation in these cases is apparently normal as long as the cortical bone is still present the periosteal surface is smooth and nothing suggests a more marked participation of the periosteum in the pathological process the latter seems to be confined entirely to the bone marrow However if there is a pathological fracture or if following operation a larger defect in the cortex has to be filled in a more adequate stimulus is exercised upon the periosteum which then reveals its normal power to osteogenesis This factor could be very well observed in both the cases

From the study of these 2 cases and from observation of Cases 13 16 18 and 20 it appears that there are certain cases of osteitis fibrosa (of the solid not cyst forming type) which show definite signs of progression and recurrence despite surgical interference They cannot be called osteitis fibrosa localisata because there is no real localization strictly speaking, it is better to speak simply of a monoossseous type of osteitis fibrosa Such cases make the usually good prognosis in cases of osteitis fibrosa somewhat doubtful

Fig 17 Case 15.

If we neglect Cases 19 and 20 in which more than one bone was involved we may state that all the other cases even if as extensive as Cases 21 and 22 were monoseous lesions with essentially normal blood chemistry There was nothing to suggest a metabolic disorder on the basis of which the bony lesion could have developed We must assume local irritative factors in the bone marrow *which lead to the characteristic picture of* osteitis fibrosa. The presence of more than one circumscribed lesion in different parts of the skeleton, however makes it not unlikely that at least for a number of cases a certain predisposition of the skeleton to fibrocystic osteodystrophy has to be assumed, probably upon an embryological basis.

This is even more so if we find cases in *which the distribution of osteitis fibrosa follows* certain anatomical structures which make it certain that the lesion must be caused by intrinsic (endogenous) and not extrinsic factors as for instance trauma. We had the

c

Fig 7 Case 25 Female, 2 years old Diffuse involvement of the left femur less marked of left tibia *Strictly unilateral*

opportunity to study 3 cases (Cases 23 24 and 25) with strictly unilateral distribution of the *dystrophic lesion. One case had been* previously reported by one of the authors (*E. Freund*) and the term osteodystrophia fibrosa unilateralis was suggested for this type of lesion We report here briefly the case again.

Case 23 A 13 year old girl, at age of 5, began to limp When 6 years old she fractured the left femur There was solid bony union after 1 year of traction and fixation in a plaster cast. Her mother stated that the left leg had been bowing progressively during the last years On physical examination we found a well developed white girl with marked asymmetry of the face and extremities Especially the left lower extremity showed a marked anterior and varus bowing X-ray pictures of the skull, spine, pelvis, and bones of the right extremities did not reveal pathological changes The left femur revealed definite hyperostotic porotic changes involving almost the entire diaphysis Only in the distal end and in the upper epiphysis could normal bone structure be seen There was an almost uniform and equal thickening of the diaphysis The cortical bone was markedly *thinned out* and formed only a very thin bony layer which, however, in no place was completely interrupted The surface of the diaphysis was smooth, and there were no signs of active periosteal bone apposition The shadow of the bone was cloudy and porotic only in a few places could a definite structure be seen These areas probably represented areas of spongy bone where the pathological changes had not yet appeared The picture was *that of diffuse* osteoporosis without cyst formation. In addition to the marked increase in *thickness, the diaphysis* showed also a distinct increase in length (three-fourths inch) despite some bowing in the middle third There were no signs of recent or healed fractures

Lesions similar to those of the humerus were seen in the diaphysis of the left radius and in the bones of

the thumb Essentially the same structural changes were also present in the left femur, only the epiphysis of head and greater trochanter, the distal metaphysis and condyles were spared Of both bones of the left leg, only the tibia was involved Almost the entire diaphysis showed the same hyperostotic porotic process which led to an increase of thickness and length, resulting in bowing of the tibia There was marked valgus deformity at the junction of middle and upper thirds The changes in the left foot corresponded to those in the left hand, the bones of the big toe only were involved There was also some irregularity in the bony structure of the first cuneiform bone and possibly of the scaphoid. But it was difficult to ascertain whether these changes were due only to atrophy resulting from disuse

For further information, a biopsy was performed at the junction of middle and lower thirds of the left tibia The histological picture was that of osteitis fibrosa Blood chemistry showed normal values (calcium 11 1 milligrams and phosphorus 3 9 milligrams), phosphatase were increased to 32 5

Because of the roentgenological and histological findings von Recklinghausen's osteitis fibrosa was considered as a diagnosis and the parathyroid glands were explored No parathyroid adenoma was found. The two lower parathyroid glands were removed The histological findings were normal

A corrective oblique osteotomy was performed with the electric saw, in the same manner as in Case 20 There was not good bony callus formation before 6 months The patient showed good correction of the deformity and was walking in a hip spica brace Frequent roentgenological control examinations did not show appreciable changes since first admission

CASE 24 A woman, 23 years of age, when 8 years old fell 4 feet and broke the right humerus in two places This healed with deformity in normal time At the age of 10 she was thrown from a horse and fractured her right wrist and the lower end of the right humerus This healed in 4 to 5 weeks She hurt the upper end of the forearm 3 months before admission and had had pain for 1 week At that time she was seen in the hospital and showed, on physical examination, a bowing of the right humerus with two bulbous enlargements of middle and lower thirds of the shaft. There was no other deformity in any other portion of the skeleton, no asymmetry of the face Roentgenograms were taken of the whole skeleton but have been discarded since They were reported as negative except for the right humerus, right radius, and right thumb A diagnosis of osteitis fibrosa cystica was made and at that time no special kind of treatment seemed to be indicated At the age of 23 she returned with a fresh fracture of the right humerus at the junction of middle and lower thirds She stated that in the meanwhile she had attended a course in nursing in Chicago During this course she fell and fractured the shaft of the right radius The arm was immobilized in a plaster cast, and the fracture healed within 4 weeks Possibility of hyperparathyroidism was considered and the patient received four X-ray treatments to the neck region She was in the best of health and without any symptoms from her right arm until she fractured the right humerus a day before admission The fracture was set, and she was put in a shoulder spica There was good callus formation in 6 weeks Blood chemistry showed normal values (serum calcium 10 7 milligrams, phosphorus 3 4 milligrams, and phosphatase 5 4 milligrams)

Roentgenograms were taken of all bones of the body but pathological changes were found only in the right upper extremity, and here only the bones of the outer side were involved humerus, radius, and bones of the thumb

The humerus was considerably enlarged The enlargement was mainly due to thickening, but there was also some real lengthening Measurements of the roentgenograms showed the right humerus to be 15 inches long, the left being only 14 inches long If one considered the existing lateral bowing of the right humerus, then the difference in length became even more marked The upper and lower epiphyses of the right humerus showed perfectly normal shadow, the entire diaphysis, however, was altogether pathological The cortical bone was thinned out very considerably, especially in the outer side, but in no place entirely interrupted In some places it was difficult to speak of a real cortex The bony shadow ended sharply toward the surrounding soft tissues The periosteal surface was smooth, the diaphysis was remarkably thickened The middle of the diaphysis was 2 inches in diameter versus ¾ inch on the normal, left, side The bony structure can be called a diffuse osteoporosis with an even more marked degree in the lower half There, one may even speak of a cystic area from the roentgenological point of view Where the more solid bone tissue bordered at the cystic area, there one could still see two transverse lines of increased density, suggesting the places where previously pathological fractures or infractions had occurred Bony trabeculæ could be made out on the inner concave side where they even showed a certain static arrangement, whereas most of the porotic areas appeared in a more diffuse cloudy shadow The normal outline of the humerus spoke against active periosteal bone production, but one found at the upper third of the outer cortex definite signs of periosteal bone formation in form of a layer of porotic bone tissue at the surface of the old cortex

The only bone of the forearm which was involved was the radius The changes were very similar to those of the humerus, but not as extensive The upper third appeared blown up to about twice its normal size The cortex was markedly thinned out or had even disappeared entirely Nevertheless, there was a sharp outline of the bony shadow everywhere The bony structure of the upper third was again of the same hazy, cloudy structure without definite signs of bony trabeculation, but the whole area did not exactly give the impression of being cystic. The

cloudy shadow extended up in the head of the radius but, in the anteroposterior view one found a narrowed zone of normal bone structure in the subchondral region. The proximal blown-up area was separated from another focus in the distal third by a kind of hour-glass constriction of ¼ inch length, where the bony structure seemed to be more normal. The distal focus was almost 4 inches long, ¾ of an inch wide and rather sharply outlined, almost of cyst-like appearance. The cortex was thinned out, shell-like, but in no place interrupted. The distal epiphysis showed perfectly normal bony structure. There was no increase in the length of the radius.

All the carpal bones had normal bone shadows. The first metacarpal bone showed thickening with the same irregular cloudy bony shadow eccentric atrophy of the cortex, and instead of the normal biconcave shape a diffuse bulging. The proximal epiphysis was of normal bony structure, the distal end, however, showed the same pathological structure as the diaphysis, which agreed very well with the absence of a distal epiphysis in the first metacarpal bone. Similar changes were also present in the first phalanx. Here, too, the proximal end was spared but the bony surface was increased in thickness. No definite changes were present in the distal phalanx.

This description was taken from plates which were sent us by courtesy from the X ray Department of St. Luke's Hospital of Chicago. Pictures taken at re-admission to the hospital showed essentially the same changes, with a fresh transverse fracture through the middle of the diaphysis of the humerus.

From the roentgenological appearance there can be no doubt that Case 24 represents the same pathology as Case 23. The roentgenograms of the involved upper extremities are almost identical. The difference between both cases lies only in the fact that Case 24 showed involvement of the upper extremity alone whereas Case 23 revealed the same pathological changes in the left upper and lower extremities. Case 24 represented only a monomelic type of this unilateral lesion without any changes in the face. Monomelic changes without asymmetry of the face were also present in Case 25 which with its involvement of only femur and tibia, forms a very welcome pendant to Case 24 the one representing the monomelic form of the upper the other of the lower extremity.

Case 25. Patient, a 22 year old woman, was admitted to the hospital for an appendectomy. She complained also of pain in the left hip of 18 years' duration. The pain was intermittent and when more severe, she was forced to limp. There was no history of trauma or fracture. On physical examination, a slight atrophy of the left lower extremity was found, but there was no difference in length. The leg was perfectly straight, but the femur showed diffuse bony enlargement and was tender on pressure. There was no soft tissue swelling. Blood chemistry normal (calcium 9.2 milligrams, phosphorus 3.3 milligrams). Roentgenograms disclosed pathological changes only in the left femur and tibia all other bones of the skeleton were perfectly normal.

Left femur showed a very extensive involvement of the diaphysis, leading to a very irregular picture of hyperostotic porotic changes. Only a small portion of the lower third of the diaphysis was spared, all the epiphyses appeared in perfectly normal bony structure. This could be seen especially well at the junction of the neck of the femur with the head and greater trochanter. There was a sharply cut borderline between healthy and pathological bone tissue corresponding exactly to the site of the previous epiphyseal plates. The porotic changes led to complete removal of normal bony tissue with formation of a very coarse, porotic, bony structure with more circumscribed areas of increased osteoporosis of cyst-like appearance. These changes were associated with expansion of the bone so that in the upper half the left femur was twice the size of the right. The cortical bone showed irregular thinning out from within, frequently to a paper-thin shell of bone. Still, the outer surface of the femur remained smooth; there were no signs of more marked periosteal reaction, although the thickening of the shaft must have occurred by very slow periostal bone proliferation. The inner structure could best be described as pseudocystic. There were no definite signs of fracture, but some coarser reinforced transverse lines of bony trabeculation, especially at the junction of upper and middle thirds, were suggestive of callus formation. An irregular area of grape like calcification was present at the junction of middle and lower thirds, where a calcified chondromatous mass could be considered. Otherwise, however, the picture was entirely different from that of skeletal chondroma.

From the anatomical distribution of the bone involvement in these 3 cases, it is quite evident that we deal with a multiosseous systemic affection of the skeleton. Pathological changes occur along certain rays. In the upper extremities only the humerus, radius, and bones of the thumb are affected. And, similarly in the lower extremity only the femur tibia, and bones of the big toe are affected. All other bones are perfectly normal. Unilaterally therefore, means not that all the bones of the affected extremity are involved, but also that even the involved bones do not show pathological structure in all their

portions Very characteristically, the epiphyses are constantly spared and the diaphyses show variable degrees of extension of the pathological changes This is also true after the bone growth has stopped and the epiphyseal disc has disappeared, as shown in Cases 24 and 25, both about 22 years old One has, therefore, to conclude that we deal here with a purely diaphyseal pathology, evidently with disturbance of the endosteal bone formation and without participation of the periosteum There is nothing to suggest a disturbance of the enchondral ossification The bone production at the epiphyseal discs seems to occur quite normally It even appears that there is increase in length growth, probably due to the hyperemia of the bone marrow of tibia and fibula This could also be observed in Case 20, which showed multiple involvement Pathological changes seem to become manifest with the so called "internal molding resorption" which removes the primary spongy bone, replacing it with mature lamellar bone of static arrangement, in normal cases In the affected bones of the 3 unilateral cases, however, the internal molding resorption, for some unknown reason, instead of leading to the formation of lamellar bone produces fibrous bone marrow with fibrous porotic spongy bone The process is evidently of very long duration and only of slow progress In all the cases it started apparently in early childhood and gradually involved the diaphyses From the roentgenograms of the tibia of Case 25, it appears that the pathological changes in the affected bones do not develop from one center with gradual involvement of the surrounding healthy bone, but they start apparently simultaneously in different foci which first are separated but may merge later and give the picture of a diffuse involvement

In the article referred to an attempt was made to define the term of osteodystrophia fibrosa unilateralis as well as possible and to rule out certain other bone diseases with which it has a number of symptoms in common Especially Ollier's dyschondroplasia had to be ruled out because of the unilaterality of the disease and the asymmetry of the face Ollier's disease, however, represents an intrinsic disturbance of enchondral ossification with formation of chondroma-like tumor masses at the site of the metaphyses It is observed within the first year of life and usually leads to marked deformity and shortening of the affected extremities In our cases clinical symptoms did not develop until after the fourth year of life in Case 25, the fifth year in Case 23, and the eighth year in Case 24 Real shortening as in Ollier's disease could not be observed On the contrary, the involved bones in 2 cases tended to increase in length, and there was a real lengthening if secondary more marked bowing of the softened bones did not occur Besides this, the roentgenological appearance of the affected bones was altogether different from that in Ollier's disease They lacked entirely the coarse structure in the metaphyses with the characteristic club-like enlargement They showed a more or less extensive involvement of the diaphyses only, with changes which best can be described as hyperostotic-porotic without participation of the periosteum Against Ollier's disease spoke also the absence of cartilaginous tissue in the piece of tibia removed from Case 23

On the basis of the findings in Cases 24 and 25, another systemic skeletal lesion has to be considered from the differential diagnostic viewpoint, and this is the melorheostose Léri This was not done in our first article because of the unilaterality of Case 23, all the cases of melorheostosis showing only involvement of one extremity in which a number of bones (never all) become changed in a very peculiar way Léri compared the appearance of the involved bones very adequately with the flow of the melted wax along the surface of a candle There is, similarly as in our cases, a certain ray distribution of the pathological process, the flow, for instance, starting with the scapula, running down the humerus, radius, thumb, or third finger By the way of distribution and by its monomelic appearance, melorheostosis has certainly a strong resemblance to our Case 24 This differs, however, quite considerably because of a number of other symptoms Melorheostosis, as a rule, affects male adults The average age of a great number of cases reported in the literature is 15½ years The roentgenological

appearance is very typical, consisting in an osteosclerotic process which affects epiphysis as well as diaphysis, endosteal bone as well as periosteal bone, leading especially by the latter to the irregular thickening of the bones with drop-like prominences on the periosteal surfaces. Our 2 cases were both very young girls when the process started and the X-ray picture is characterized by the hyperostotic porotic change, which means that the affected bones show cloudy shadows (porosis) with diffuse or spindle shaped widening (hyperostosis). So despite the monomelic affection and peculiar systemic anatomical distribution, melorheostosis can safely be ruled out.

RELATION OF OSTEODYSTROPHIA FIBROSA UNILATERALIS TO COMMON OSTEITIS FIBROSA

Remains the discussion of the relation of osteodystrophia (osteitis) fibrosa unilateralis to the more common type of osteitis fibrosa cases. They have in common the histological findings. We have, however in our previous article stressed the point that the histological picture of osteitis fibrosa cannot be taken as a specific reaction of the bone marrow. We know that the same changes may occur under quite different stimuli and so the histological diagnosis of osteitis fibrosa may frequently be misleading and obscuring. In both of our cases, however certain roentgenological signs, especially the apparent cyst formation led to the first clinical diagnosis of cystic osteitis fibrosa. In Case 23 at time of first admission only X-ray pictures of the pelvis were taken (all the clinical symptoms pointed to the left hip) and so the diagnosis is quite justifiable. In Case 24 pictures were taken of all the bones of the body and a multiple "cystic" lesion was recognized. The extensive involvement of the bones, of course, speaks primarily and decidedly against a localized lesion of osteitis fibrosa. The multiple bones affected suggested generalized osteitis fibrosa in the sense of von Recklinghausen's disease or hyperparathyroidism, although the systemic distribution with unilateral or monomelic manifestation speaks *a priori* against a central cause. Blood chemistry in all 3 cases was essentially negative, especially as far as the calcium and phosphorus values were concerned. Nevertheless, in Case 23 an exploratory operation of the parathyroid glands was performed, two glands being removed with perfectly normal microscopic and macroscopic appearance. In Case 24 the neck region was irradiated with X-ray without any changes in the skeleton.

It is quite certain that both cases have essentially nothing to do with generalized osteitis fibrosa. Against it speaks the age (Recklinghausen's disease is not observed in childhood) the roentgenological appearance (Recklinghausen's disease leads to marked general osteoporosis of the skeleton with cyst formation and brown tumors hyperostotic changes take place only at the site of pathological fracture our cases showed very characteristic hyperostotic porotic changes with systemic unilateral or monomelic distribution. There were no definite signs of real cyst formation) and finally the normal clinical findings with absence of general symptoms.

Thus, it seems that osteodystrophia fibrosa unilateralis deserves an independent position among the osteitis fibrosa cases. And, as a matter of fact, this was also the conclusion in the paper referred to. However since the observation of Cases 24 and 25 which can be considered as less extensive unilateral cases, it is theoretically possible to assume that there are different degrees in extension of fibrous osteodystrophy. One could think that in the same way as Cases 24 and 25 monomelic distribution represents a reduction of a strictly unilateral manifestation, the extensive monoosseous cases represent less extensive degrees of monomelic forms and, finally that the localized lesion could be considered as the mildest form in the development of fibrous osteodystrophy. Case 25 especially with the changes in the tibia just in the beginning and the bones of the foot perfectly free, is a very welcome link in the chain of different manifestations of fibrous osteodystrophy. It stays between the monomelic case (Case 24) and the monoosseous diffuse form (Cases 21 and 22). Such an assumption is, of course, very hard to prove since we know so little about the etiology of fibrous osteodystrophy. But it does not seem entirely artificial if one considers the very marked regularity in the distribution of our 2 cases in which, as far as the

upper extremities are concerned, the lesions resemble each other like one egg another Furthermore, the typical localizations of the localized monosseous type would also fit very well in this conception of a primary endosteum lesion It really must be quite surprising to find the upper metaphysis of the humerus, femur, and tibia so often involved without thinking of a certain intrinsic predisposition of these portions to fibrous osteodystrophy It is always a metaphyseal or diaphyseal lesion without primary participation of the periosteum Even after disappearance of the epiphyseal plates, the borderline between epiphysis and diaphysis remains strictly observed It is a disturbance of endosteal bone formation in the diaphysis which starts apparently most frequently in the juxta-epiphyseal portions where the primary spongy bone in normal cases is transformed to mature lamellar bone tissue Of what kind this disturbance is, if the simple traumatic factor is unable to solve the problem, it is impossible to say with our present knowledge of bone formation and bone growth It has to be admitted that trauma may facilitate the development of such a lesion, but it cannot be the real etiological factor To our knowledge, all the experiments undertaken to cause localized osteitis fibrosa by trauma and intermedullary trauma have failed In most of the clinical cases the onset is insidious and, when fractures occur, they are, as a rule, pathological, developing in the diseased and weakened skeletal portions All the cases have in common the relatively benign clinical course which in the localized cases may lead even to spontaneous healing The more extensive cases are, of course, not as favorable as far as prognosis is concerned, they even resist quite often radical surgical procedures, showing marked tendency to recurrence The unilateral cases, however, are at present entirely inaccessible for treatment, except for a symptomatic one in cases of complications

Summarizing, we can say for the group of osteitis fibrosa There are localized cases of a solid or cystic type, usually situated in the upper portion of the diaphysis of the humerus, femur, and tibia, less frequently, diaphyseal localization is observed, never localization in epiphyses Besides the localized form, more extensive cases can occasionally be seen with involvement of the greater part of the diaphyses Multiple localized lesions are rare but may occur without any apparent rule in the distribution of the lesion There is a strictly unilateral (monomelic) form of fibrous osteodystrophy with involvement of the entire or of great portions of the diaphyses of bones arranged in longitudinal ray-like anatomical distribution On the basis of such observations, it is believed that the localized form represents an abortive type of the extensive monosseous form The latter is an abortive form of the monomelic type which, in turn, is considered as an abortive form of the unilateral osteodystrophy Inasmuch as the latter cannot be taken as traumatic in origin, the purely traumatic etiology of all the other forms is rather doubtful All the cases mentioned have apparently no nosological relationship to the generalized form of osteitis fibrosa Von Recklinghausen's disease has to be considered as a generalized bone disease in which every part of the skeleton is affected The degree of affection may vary, according to mechanic irritative factors The distribution of cysts and brown tumors in the generalized form is irregular and does not follow certain rules Disturbance of calcium metabolism and tumor formation in parathyroid glands is demonstrable almost in every case of von Recklinghausen's disease, never in the different "localized" forms of fibrous osteodystrophy

THE RELATION OF CHRONIC MASTITIS TO CERTAIN HORMONES OF THE OVARY AND PITUITARY AND TO COINCIDENT GYNECOLOGICAL LESIONS

PART II—CLINICAL AND HORMONE STUDIES[1]

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THE first part of this study which appeared in a previous number of this journal was concerned with a consideration of possible causes and the histology of the diffuse breast diseases commonly classed under the general term of "chronic mastitis." Particular attention was devoted to the current belief in an underlying ovarian dysfunction and to an alternative theory giving nervous and vascular factors a more prominent rôle. The present paper is a continuation of this work and consists in a collection of clinical and laboratory evidence having a bearing on these two conceptions.

The clinical data for the study of chronic mastitis are based upon 261 cases of diffuse breast disease observed during the 3 year period of 1931–1933 inclusive. Of these 239 were primarily patients of the breast clinic at the Memorial Hospital whereas 22 were from the gynecological department of the Roosevelt Hospital.

CLASSIFICATION

The original 261 cases have been divided first into three groups based upon the clinical character of the disease in the breast. The histological basis of these clinical forms has already been discussed. (1) In the first group were placed the 183 cases with tender areas of induration or nodularity. Among these patients were many who complained of a temporary premenstrual swelling but none with permanent enlargement or discharge from the nipple. (2) The second group consisted of 31 patients, all of whom reported a permanent enlargement of the breasts, usually with cyclical pain and swelling but without discharge from the nipple. (3) The third group of 47 cases was made up of the patients with discharge from the nipple, which necessarily included many with pain and 6 with hypertrophy.

A secondary classification based on a gynecological history and examination was made to bring out the importance of the two *major theoretical etiological factors*, ovarian dysfunction and a nervous and vascular disturbance perhaps caused by or associated with pelvic lesions. Since the endocrine factor is more in harmony with present views, the groups given below are arranged in order of the apparent prominence of glandular dysfunction. The incidence of lesions having a possible effect on the pelvic nerves is found in the data on inflammation, parametritis, retroversion, *and cervical infections.*

The classification which has been employed is as follows:

1. Breast disease in association with cystic ovaries and menstrual abnormalities (anatomical and functional evidence of ovarian disorder).
2. Breast disease in association with cystic ovaries but normal menstruation (anatomical evidence only of ovarian disorder).
3. *Breast disease without evidence of* anatomical disease of the ovaries, but with menstrual abnormalities (functional evidence only of ovarian disorder).
   a. Prolonged menstrual cycle, 35 days or longer.
   b. Scant menstrual flow, 2 days or less.
   c. Excessive or prolonged flow, 8 days or more.
   d. Short menstrual cycle, 21 days or shorter.
4. Breast disease following hysterectomy (functional disturbance of retained ovaries).
5. Breast disease without evidence of cystic ovaries or menstrual abnormalities but with signs of inflammation or pelvic congestion (no clinical evidence of ovarian disorder).
   a. Acute and chronic salpingo-oophoritis.

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TABLE I—CLINICAL CLASSIFICATION OF 183 CASES WITH BREAST PAIN WITH NODULARITY

	Total	Age	Marital Status				Menstrual Cycle						Duration of Flow			Uterus						Parametria		Adnexa						Cervix				Thyroid	
		Average age in years	Single	Married No pregnancies	Married children only	One or more children	Normal	Long cycle 35 days or more	Short cycle 25 days or less	Irregular 25-35 days	Continuous	Amenorrhea	Normal duration	Short menses <3 days	Long menses >7 days	Normal	Retroversion 1st degree	Retroversion 2nd degree	Retroversion 3rd degree	Partial prolapse	Enterocele	Normal	Tenderness or thickening	Normal	Acute salpingo-oophoritis	Chronic salpingo-oophoritis	Previous salpingo-oophoritis	Cystic ovaries	Grey removal cystic ovary	Normal	Laceration	Erosion	Endocervicitis	Hypertrophy	No pelvic examination
1. Cystic ovaries and abnormal menses	21	29	2	2	0	7	3	1	4	1			1	7	3	1	2	2	4		1	9	2			6		9	2	1	1	4	1	1	
2. Cystic ovaries and normal menses	18	31	2	4	2	10	18						18			6	2	1	6	3	3	11	5		3	3		16	2	2	0	5	4		
3. Abnormal menses but no demonstrable cystic ovaries																																			
a. Long cycles	23	32	5	3	4	11		18		5			15	4	1	11	3	2	3		4	15	3	20		1				3	3	2	4	1	2
b. Short flow	20	33	4	2	0	14	15		2					0		2	4	5	1	3		12	5	17						7	4	3	4	1	3
c. Extensive flow	5	30	1	3	0	1	3				4				3	5					1	5	0	5								1			
d. Short cycles	25	33	1	3	0	21		15					15			4	3	5	2			4	7	13		1				4	2	4	1		1
4. Posthysterectomy	2	32				2						2										2		1						1					
5. Normal menses with pelvic inflammation or congestion																																			
a. Pelvic inflammation	9	32	0	4	2	3	9						9			4	4	1	0	0	2	6	3		1	6	2			3			2	1	
b. Pelvic congestion parametritis	24	32	1	3	2	18	24						24			10	6	6	2	2	4		3	24						5	5	9	4	1	
c. Retroversion	17	34	1	3	0	13	17						17			0	0	1	9	2		17		17							7	5	1	7	
d. Cervical infections	8	30		2		6	8						8			5	3					8		8							4	1	3		
e. Sexual factor only	3	33	1	1		1	3						3			1	1					2		2						2				1	1
6. Primary dysmenorrhea	22	25	11	1			22						22			3	1				1	4		4						3				2	8
7. Thyroid hypertrophy	4	29	1	1		2	4						4			1	2					3		3						3				4	1
8. Unclassified	12	30	6			6	12						12			5	4				1	9		9						6					3
Total	183	30.7	36	33	9	105	133	19	21	6	1	2	141	31	9	60	35	20	29	9	18	115	49	134	4	17	2	26	4	41	26	37	21	24	19

b. Chronic parametritis and pelvic congestion

c. Retroversion and partial prolapse

d. Cervical infection and hypersecretion

e. Presence of an apparent sexual relationship

6. Breast disease with primary dysmenorrhea

7. Breast disease with thyroid hypertrophy

8. Unclassifiable cases

The first four groups contain all the cases in which there were clinical signs or symptoms suggestive of an ovarian dysfunction. Group 5 includes cases without evidence of an ovarian dysfunction but with lesions in the pelvis, making an irritation of the pelvic sympathetic nerves a possibility. A number of cases with such pelvic disease showed also evidence of ovarian abnormality and have been arbitrarily classed in the dysfunction groups. The total incidence of pelvic lesions can therefore be obtained only by reference to the detailed tabulation in the charts (Tables I, II, III). Cases with no classifying feature except pri-

TABLE II—CLINICAL CLASSIFICATION OF 41 CASES WITH HYPERTROPHY OF THE BREAST

	Total	Age	Marital Status				Menstrual cycle								Duration of Flow			Uterus					Parenchyma		Adnexa							Cervix			Thyroid	
		Average age in years	Single	Married	Married and pregnant	Married and children	Long cycle 35 days or more	Long cycle 31 days or less	Long cycle 27 days or less	Short cycle 27 days or less	Short cycle 27 days or more	Normal cycle	Irregular cycle	Normal cycle	Short flow < 4 days	Normal flow 4 days	Excessive flow > 4 days	Normal size	Enlarged	Enlarged and tender	Enlarged and fixed	Enlarged and nodular	Normal	Fibrocystic	Normal	Cystic	Cystic and tender	Cystic and fixed	Cystic and nodular	Cystic and tender and nodular	Normal	Erosion	Laceration	Normal	Hypertrophy
Cystic ovaries and abnormal menses	1	30						1										1						1						1				1		
Cystic ovaries and normal menses	3	28				2	2								2			2					2	1						2	2					
3 Abnormal menses but no demonstrable cystic ovaries																																				
a. Long cycles	4	30						4										4						4								2				
b Short flow		1														1								1		1										
Excessive flow		44				1													1												1					
d Short cycles																																				
4 Postmenopausal	6	57				4					6												4		4					4	4					
5 Normal menses with prior [illegible] or congenital [illegible] Pelvic [illegible] [illegible]																																				
b Prior congenital [illegible]	4	30				3	4							4									4							4						
c. Retroversion		39												1																						
d Cervical pelvic [illegible]																																				
Sexual factor only	3	5					3										3						3		3						3					
6 Primary dysmenorrhea	3	15	3				3							3																	3					
7 Thyroid hypertrophy		15																																		
8 Unclassified																																				
Total	41	39	30	10		9	30	6			6	30		4	5	1		1	1				37	3	30		1		3	2	9		3	3		5

mary dysmenorrhea or thyroid hypertrophy have been separately grouped since these conditions may have either an endocrine or nervous significance

METHODS OF HORMONE STUDY

As patients were admitted to the clinic, typical examples were selected for hormone studies, based on four types of analysis

1 *The urinary excretion of estrin* Estrin was obtained from the urine by the chloroform extraction method of Frank (15) and assayed by injection of the extract in oil into spayed adult white mice In all except the earlier determinations, a positive reading was accepted only when full estrus occurred in three of four animals injected with the same quantity of hormone according to the plan of Siebke (53) On account of the variation in excretion at different times in the monthly cycle the total estrin excreted during a menstrual cycle was determined by the separate assay of consecutive 72 hour total urine specimens.

TABLE III.—CLINICAL CLASSIFICATION OF 47 CASES WITH ABNORMAL SECRETION FROM THE NIPPLE

	Total	Age	Marital status				Menstrual cycle						Duration of flow			Uterus						Parametria		Adnexa					Cervix				Thyroid	
		Average age in years	Single	Married. No pregnancies	Miscarriages only	One or more children	Normal	Long cycle. 35 days or more	Short cycle 23 days or less	Irregular 21–35 days	Continuous	Amenorrhea	Normal duration	Short menses. <3 days	Long menses >7 days	Normal	Retroversion. 1st degree	Retroversion 2nd degree	Retroversion 3rd degree	Partial prolapse	Fibroids	Normal	Tenderness dyspareunia	Normal	Acute salpingo-oophoritis	Chronic salpingo-oophoritis	Previous salpingo-oophoritis	Cystic ovaries	Prev removal of cystic ovary	Normal	Laceration	Erosion	Endocervicitis	Hypertrophy	No pelvic examination
1 Cystic ovaries and abnormal menses	5	33			1	4		3	2				1	2	2	1		1	2	1	2	3	2			1		5		1	1	1	1		
2 Cystic ovaries and normal menses	3	36				3	3						3						3			3							3	1	1				
3. Abnormal menses but no demonstrable cystic ovaries a. Long cycles	13	39	1	2	0	10		12		1			8	4	1	6	4	1			2	10	1	11						8			2		2
b. Short flow	3	32				3	3							3		1		2				1	2	3							2				
c. Excessive flow	1	42				1			1						1	1					1	1		1							1				
d. Short cycles	6	35	1	1		4			6				6				1	4	1			4	2	5		1				1	2	1	1		
4. Posthysterectomy	5	39	1		1	3						5										5		5					2	3		1			
5 Normal menses with pelvic inflam. or congestion a. Pelvic inflammation	1	31				1	1						1			1						1			1								1		
b. Pelvic congestion-parametritis	1	28				1	1						1					1					1	1									1		
c. Retroversion	5	32		1		4	5						5					2	3			5		5							2	1	1		
d. Cervical infections	3	34				3	3						3			3					1	3		3								2	1		
e. Sexual factor only																																			
6. Primary dysmenorrhea																																			
7 Thyroid hypertrophy																																			
8. Unclassified	1	25	1				1						1																						1
Total	47	35 6	4	4	2	37	17	15	9	1		5	29	9	4	13	5	11	9	1	6	36	8	34	1	2		5	5	14	9	6	8		3

The normal excretion of estrin during a single cycle was found by Frank (15) to vary from 800 to 1,500 mouse units, by Siebke (51) from 200 to 2,000 A peak of excretion near the time of ovulation was noted by both of these workers and a second peak shortly before menstruation by Frank (15) Control tests made upon 4 normal women in the course of this study gave a range of 760 to 2,625 and an average of 1,505 mouse units The study of the patient with the highest output was completely repeated after a 6 months' interval, the second determination showing 3,155 units The highest rates of excretion were found near the middle of the month, but occasional unexplained peaks occurred at other times

On account of the many types of menstrual disturbance reported in cases of chronic mastitis, it is important to reconsider the variations in hormone excretion that have already been reported in relation to these menstrual abnormalities Menstrual cycles of increased

length may according to Siebke (54) be of two kinds those with a period of complete rest preceding the beginning of the usual hormone cycle and those with a continuous hormone excretion, possibly with several peaks during the entire interval. Amenorrhea similarly may be of several types (Frank and Goldberger 16) varying from the practical absence of hormone in blood and urine to the excessively high levels reported in the so called polyhormonal amenorrhea of Zondek (60) The hormone basis for the short cycle has been little studied The variability of amount and duration of the menstrual flow within relatively normal limits is not according to Siebke s (52) observations dependent upon quantitative variations in the ovarian function.

2 *Blood estrin* The test of Frank and Goldberger (17) for the female sex hormone was employed for study of the presence of the hormone in the blood. The originators of the test maintain that a positive reaction, as a rule, may be obtained in normal women during the premenstrual week. This has been both corroborated (Hirsch Siebke, 51 Mazer and Andrussier) and contradicted (Janney Ford and Mueller) Experience with a short control series has shown that in our hands negative tests are not infrequently obtained during the premenstrual week, a point to be remembered in interpreting the results given below In a few recent cases the test of Fluhmann (11) based on the production of mucification of the vaginal mucosa of the spayed mouse has also been used

An increase of follicular hormone in the blood has been observed in certain types of bleeding at puberty and the menopause (Frank and Goldberger 16 and Siebke 52) High values have been found also in certain cases characterized by premenstrual nervous tension in which various vascular and nervous symptoms are prominent and dysmenorrhea with breast pain and swelling may be present (Frank 14) Low values have been found in some women with functional sterility but normal menstrual cycles (Frank 14 Mazer and Andrussier)

3 *The urinary excretion of prolan* Attempts were made to demonstrate the presence of prolan in the urine by the use of the alcohol precipitation method of Zondek (61) and the benzoic and tungstic acid methods of Katzman and Doisy (27 29) Extracts by the two latter methods were prepared by and under the direction of Dr Helen Downes of the department of chemistry of the hospital. These tests also were carried out upon a series of urines obtained at 3 day intervals throughout the menstrual cycle

Previous estimations of the daily prolan output of normal women have varied widely Zondek (64) reported 8 units per day in the postmenstruum 25 in the interval 29 in the premenstruum and 25 during menstruation Katzman and Doisy (28 29) found a maximum excretion of 12 to 16 mouse units at about the time of ovulation and sometimes a rise during menstruation with the amounts between these times falling to three mouse units, one rat unit, or less. Other workers have reported only traces of prolan in the urine of normal women.

These conflicting results are undoubtedly due to variations in technique One of the most important is found in the particular physiological reaction taken as the measure of a unit there being two commonly employed. These are first the direct effect on the ovarian follicle second the indirect effect on the tubular tract, in particular the opening of the vaginal introitus and the production of the estrus type of vaginal smear The latter appears more reliable but undoubtedly requires much more hormone than is needed to produce slight follicular changes.

Tests on the urine of normal women with extracts concentrated to show from 5 to 10 units of prolan per liter when injected into infantile mice were found by us rarely to produce opening of the introitus and never full estrus. Evidence of partial ripening of the follicles was frequently present in the serial sections of the ovaries but was difficult to evaluate for comparative purposes.

A great increase of prolan excretion has been found in the presence of certain malignant tumors, such as choriocarcinomas and teratoma, and a slight increase has been reported in the presence of other new growths especially those of the female genital organs

TABLE IV —REPRODUCTIVE HISTORY

	Cases with pain	Cases with hypertrophy	Cases with secretion
	183	31	47
	Per cent	Per cent	Per cent
Single women	19 2	32 3	8 5
Married—childless	17 5	32 3	8 5
Miscarriage only	4 9	6 5	4 3
One or more children	57 9	29 0	78 7

TABLE V —MENSTRUAL DISTURBANCES

	Cases with pain	Cases with hypertrophy	Cases with secretion
	183	31	47
	Per cent	Per cent	Per cent
Normal menstruation	58 5	48 1	29 7
Amenorrhea after hysterectomy	1 1	19 4	10 7
Abnormal menstruation	40 4	32 2	59 6

(Zondek, 63, Hamburger) Besides these neoplastic conditions, an increase in prolan excretion occurs in women with marked degrees of ovarian deficiency, particularly in the menopause (Zondek, 61, 62, Oesterreicher, Lassen and Brandstrup) In the amenorrheas of long standing in young women, the hormone has been occasionally found (Zondek, 60, Kaufmann and Muehlbock), but in the milder forms of ovarian hypofunction its presence has not been proved Besides these ovarian conditions prolan has been reported in cases with certain diseases of the central nervous system (Kraus) and migraine (Riley, Brickner, and Kurzrok) These points are of importance on account of the delayed and scant menstruation and headaches (Whitehouse) noted in cases of the painful breast

4 Serum prolan The test of Fluhmann (10), consisting of the simple injection of small amounts of blood serum into infantile mice is capable of demonstrating prolan when it is present in relatively large amounts in the blood stream Blood from normal women never produces a vaginal reaction, although possible follicular changes may be observed This test was likewise applied to a series of mastitis patients at weekly intervals Fluhmann (10) found prolan A in the blood of certain patients with prolonged amenorrhea, but obtained negative results in women suffering from the minor degrees of hypo-ovarianism, as manifested by persistently delayed menses, scanty menses, and short periods of amenorrhea

5 Examination of the endometrium The uterine mucosa of any patient is an extremely sensitive indicator of her ovarian function, subject to none of the indirectness or loss inherent in any method involving extraction and reinjection For that reason the evidence afforded by examination of endometrium from 31 cases of breast disease is especially important

RESULTS OF THE CLINICAL AND HORMONE STUDY

The evidence having a bearing on the etiology of chronic mastitis has been assembled under thirteen headings

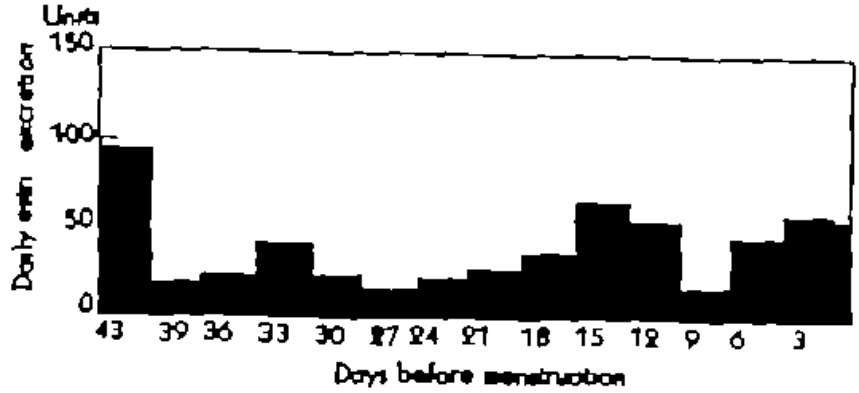
1 Age incidence The average age of the patients with pain was 30 7 years, those with hypertrophy 29 1 years, and those with secretion 35 6 years

2 Reproductive history (Table IV) A contrast is afforded here between the cases with hypertrophy, nearly two-thirds of which were childless, and those with secretion, the great majority of whom had borne children

3 Menstrual history The frequency of menstrual disturbance in cases of chronic mastitis has heretofore been the chief clinical evidence of an ovarian dysfunction The total incidence of abnormalities in the frequency or duration of the menstruation is shown in Table V

a Disturbances in the cycle of menstruation (Table VI) were most common in the cases with discharge from the nipple and were usually of the delayed period or prolonged interval type

The daily excretion of estrin in the long cycle cases of this study averaged less than those with a regular rhythm (Tables IX A IX B, IX C, IX D) but Zondek (60) in particular has reported the reverse in the so called polyhormonal amenorrhea in which there may be breast symptoms An example of the estrin



Graph Total estrin excretion in the 43 day cycle of patient with non-puerperal secretion from the nipples Lxp 166 Total units 1,743

excretion in the prolonged cycle type is shown in graph 1, obtained from the following case

CASE 1 S. W Patient was admitted to hospital February 16, 1934. She was 34 years of age, married and had two children, ages 7 and 3½ years Menstruation had always occurred at 6 to 8 week intervals with a 5 day normal flow and no dysmenorrhea No discomfort had ever been felt in the breasts until 2 weeks before admission when a discharge was noted from the left nipple. Examination showed the breasts medium in size, dependent in shape, with wide slightly congested areolæ, and a moderate diffuse nodularity in both outer quadrants A little oily discharge could be expressed from the left nipple, and at a later visit some was obtained from the right also. By vaginal examination, the fundus was found slightly retroverted and enlarged with a moderately hypertrophied and eroded cervix and a slight enlargement of the right ovary

Hormone tests The excretion of estrin amounted to 1 743 mouse units in 43 days Three blood serum specimens tested by the Fluhmann method for estrin were negative No increase in prolan was found in 3 serum specimens or in 14 specimens of urine extracted by the tungstic acid procedure of Katzman and Doisy

TABLE VI.—DISTURBANCES IN THE CYCLE OF MENSTRUATION

	Cases with pain	Cases with hypertrophy	Cases with secretion
	18	33	47
	Per cent	Per cent	Per cent
Normal cycle	72 7	6 3	36
Amenorrhea after hysterectomy		39 4	19 6
Long cycle—35 or more days	10		3
Irregular cycle—11 to 35 days	3		
Short cycle—9 or fewer days	11 1		10
Continuous bleeding			

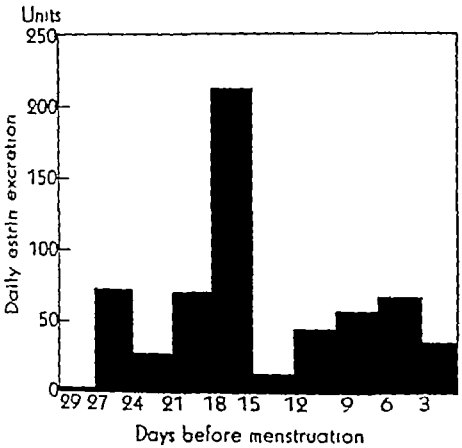
b Disturbances in the duration of the menstrual flow (Table VII) A decrease in the amount of the menstrual flow in the cases of painful breast has been described repeatedly and was noted in 16 9 per cent of the patients of this series It was also common with secretion from the nipple

Since the scant periods have been cited as evidence of an underfunction of the ovary It is interesting to note that the monthly estrin excretion in 6 women with periods of less than 3 days was not below the general average (Table IX B IX C) An example of the estrin excretion in a woman menstruating for only 1 day is shown in Graph 2 The history of this case follows

CASE 2 T J Patient was admitted to hospital February 2 1935 She was married, age 36 years, with a history of one normal delivery 2½ years, and a therapeutic abortion 1 year before admission Menstruation had formerly been of the type, 28, 3½ average, without pain, but since the birth of her child the periods had gradually been reduced to a very scant flow of 1 day's duration and became associated with headache, dizziness, and dysmenorrhea

Three months after the delivery of her child her left breast had been removed by radical mastectomy for carcinoma For 3 months before her admission to the Memorial clinic there had been marked pain in the right breast, chiefly premenstrual, with hypersensitivity of the skin of the axilla, right shoulder and arm, and occasionally of the right leg In addition there was some weakness of the right hand, with general nervousness, anxiety headache and dysparenia

Examination showed the right breast small, dependent, and slightly nodular in the outer quadrants The uterus was normal in size, in midposition, with tenderness elicited by its motion. The adnexa were tender and the cervix large.



Graph 2 Total estrin excretion in the 29 day cycle of a patient with painful breasts and a menstrual flow of 1 day Exp 103 Total units 1,756

The case was treated for 4 months with theelin without success and then selected for hormone study No abnormalities were noted in the prolan or estrin content of either blood or urine

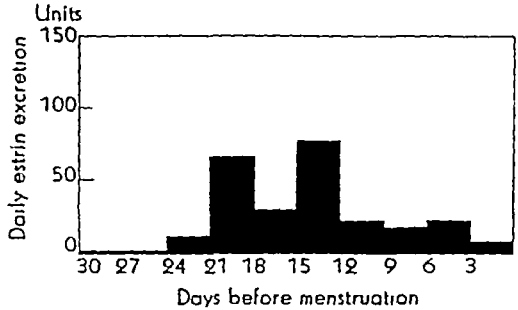
Hormone tests The excretion of estrin amounted to 1,756 mouse units in 29 days Four blood tests (Frank and Goldberger, 17) gave a single positive reaction in the third week There was no evidence of increase in prolan in 3 specimens of serum or in 9 of urine extracted by the tungstic acid method

Diminished menstruation cannot therefore be accepted as necessarily a sign of ovarian underfunction and may be dependent on a local pelvic or uterine abnormality The dyspareunia and pelvic pain in this case will recall the fact noted in the first section of this paper that a diminishing menstruation has been ascribed to a chronic parametritis

c *The appearance of breast symptoms after hysterectomy* was noted in 12 cases In all of

TABLE VII —DISTURBANCE IN THE DURATION OF THE MENSTRUAL FLOW

	Cases with pain	Cases with hypertrophy	Cases with secretion
	183	31	47
	Per cent	Per cent	Per cent
Normal flow	77 1	64 5	61 7
Amenorrhea after hysterectomy	1 1	19 4	10 6
Short flow—less than 3 days	16 9	12 6	19 1
Long flow—more than 7 days	4 9	3 2	8 5



Graph 3 Total estrin excretion during 30 days in a patient with breasts painful following hysterectomy Exp 155 Total units 762

these there was satisfactory evidence that one or both ovaries had been retained, and in the urine of all cases studied estrin was demonstrable An example of the cycle of estrin excretion after hysterectomy is shown in Graph 3

CASE 3 K Patient was admitted to hospital September 11, 1931 She was married, 35 years of age, with two children, ages 12 and 2 years, and a history of one miscarriage 5 years before admission The symptoms at first consisted in irregular uterine bleeding and a lump in the right breast During the following 3 years the patient underwent four operations a myomectomy, the excision of a fibroadenoma, a curettage, and finally a supravaginal hysterectomy The ovaries were noted as normal at the last operation, although no special attention was given them by the surgeon

Following her operation, the patient noted an increase in pain and swelling of her breasts, symptoms which appeared to undergo cycles of exacerbation Examination of the breasts 11 months after the operation showed them to be nodular in their outer quadrants

Hormone tests The excretion of estrin amounted to 762 mouse units in 30 days Four blood serum specimens tested by the Fluhmann technique gave one weak reaction No definite increase in prolan was found in 4 serum specimens or in 10 specimens of urine extracted by the tungstic acid method

TABLE VIII —OVARIAN CONDITIONS OBSERVED AT OPERATION

	Cases with pain	Cases with hypertrophy	Cases with secretion
Follicle cysts	19	4	6
Cystic corpora lutea	3	0	3
Salpingo-oophoritis	4	0	1
Miscellaneous	9	3	2
Normal	8	3	3

Fig. SC8597. Follicle cysts and papillomas of the ovary in a case with pain and swelling of the breasts and secretion from the nipples.

Besides these benign cases, 11 instances of breast cancer following hysterectomy have been observed by the writer during the last 5 years, although no systematic search of the hospital files has been made. It is of incidental interest that Aschner maintains that a special tendency to cancer exists in the breasts of women who have had their uterus removed and includes this danger among his reasons for preferring *myomectomy to hysterectomy* for the treatment of uterine fibroids.

The reason for the development of breast disease after hysterectomy is not clear. An ovarian dysfunction based on cystic changes developing in the retained ovary is a possibility although recent experimental work has not strengthened the accepted clinical belief in such a process (Sessums and Murphy). One study, that of Kosakaé, Ohga and Okamoto, has reported an increase in estrin excretion after hysterectomy perhaps due to the failure of the endometrium to utilize its quota of hormone. In 2 cases completely studied by us, no increase in estrin excretion was found, *although high values were obtained in a third* patient from whom, however, only a series of 8 discontinuous 24 hour specimens could be procured. It must finally be pointed out that the pelvic plexus of sympathetic nerves must unquestionably be affected by the removal of the uterus and the subsequent inflammatory and reparative processes. The sudden appearance of milk shortly after supravaginal hysterectomy with preservation of an ovary *suggests therefore the possibility of a nervous* as well as an endocrine factor in the following case.

CASE 4. C. B. Patient was admitted to the Roosevelt Hospital, March 28, 1934. She was a married colored woman of 37 with one child 12 years of age, and one miscarriage [illegible] years before admission.

A supravaginal hysterectomy was performed for a large fibroid uterus and a right salpingo-oophorectomy for fibrous and cystic degeneration of the ovary. Pathological sections showed normal endometrium consistent with the twelfth day of the cycle and an adenomyosis of the inner layers of uterine musculature.

The postoperative course was normal but, on the ninth day, the patient reported that both breasts

TABLE IX A.—TOTAL ESTRIN EXCRETION IN THE CYCLE OF 5 NORMAL WOMEN

Experiment number	Menstrual Date	Pelvic pathology	Menstrual [illegible]
	[illegible]	Normal	[illegible]
1	[illegible]	Normal A	[illegible]
Repeat 1	[illegible]	Normal B	
[illegible]	[illegible]	Normal	[illegible]
6	[illegible]	Normal	[illegible]
7	[illegible]	Normal	[illegible]
Average			[illegible]

TABLE IX B.—TOTAL ESTRIN EXCRETION IN THE CYCLE OF 7 WOMEN WITH PAINFUL NODULAR BREASTS

Experiment number	Menstrual Date	Pelvic pathology	Menstrual [illegible]
[illegible]	[illegible]	Palpable cyst ovary	[illegible]
	[illegible]	Premenstrual [illegible]	[illegible]
[illegible]	[illegible]	Premenstrual [illegible]	[illegible]
[illegible]	Amount [illegible]	Pelvic structures. Both ovaries present	[illegible]
8	[illegible]	Complete [illegible]	[illegible]
[illegible]	[illegible]	Normal pelvis	[illegible]
[illegible]	[illegible]	Bilateral oophorectomy for pseudomucinous cyst	[illegible]
Average			[illegible]

were secreting milk in copious amounts This continued for 8 weeks at which time the secretion was noted as diminishing and much thinner A month later the patient returned complaining of pain in the left shoulder and neck. Examination showed a complete cessation of secretion from the breasts, a normal vagina without evidence of atrophy and a slightly enlarged left ovary

Hormone tests On the sixteenth day after operation a 24 hour specimen contained 108 mouse units Nine specimens examined during the next 6 weeks showed 24 hour excretions of 0 to 28 units Seven specimens examined during this period for prolan by the alcohol and tungstic acid methods showed no increase over the normal

d The connection between menstrual abnormalities and breast symptoms was emphasized by the fact that in 82 patients the onset of the breast and menstrual symptoms was practically simultaneous The menstrual change was a decrease in duration or frequency in 62 of these cases (Table XI)

4 Ovarian pathology in cases of chronic mastitis (Table VIII) From 21 cases observed at operation by the writer and from reports of the pelvic pathology of 47 further cases operated upon by other surgeons, one can find evidence of a relatively high incidence of cystic disease of the ovary

For many years a condition sometimes termed pseudopregnancy and characterized by delayed menstruation with as a rule breast changes has been recognized The symptoms are usually attributed to a persistent or cystic corpus luteum (Halban, Reeb), although Zondek (60) has shown that a persistent follicle may produce the same results On account of an increase of folliculin in the urine and in the cyst of the ovary of his patient, Zondek (60) proposed the name polyhormonal amenorrhea for these cases In another case with colostrum in the breasts and lutein cell cysts in the ovaries Kaiser found the Aschheim-Zondek test to be positive Case 5 apparently belongs to this group

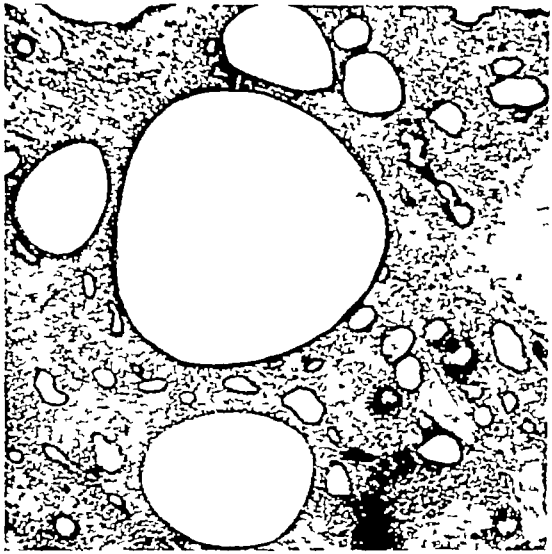


Fig 2 SD9573 Endometrial hyperplasia in a woman of 42 with normal breasts

CASE 5 H G Patient was admitted to the Roosevelt Hospital, June 19, 1933 She was a mar-

TABLE IX C—TOTAL ESTRIN EXCRETION IN THE CYCLE OF 6 WOMEN WITH PAINFUL BREAST HYPERTROPHY

Experiment number	Menstruation	Pelvic pathology	Mouse units
3	36 2	Salpingo-oophorectomy for cyst and inflammation	095
41	30 1½	Partial oophorectomy for cysts	2300
Repeat 41	8 2	Partial oophorectomy for cysts	835
111	8 1	Salpingo-oophorectomy for cysts and inflammation	710
34	2 8	Possible endometrial hyperplasia	3000
111	31 5	Operation for salpingitis parametrial tenderness	1955
11	30 7	Parametrial tenderness	1-65
Average			2170

TABLE IX D—TOTAL ESTRIN EXCRETION IN THE CYCLE OF 7 WOMEN WITH ABNORMAL SECRETION FROM THE NIPPLE

Experiment number	Menstruation	Pelvic pathology	Mouse units
16	41 4	Partial oophorectomy for cystic corpus luteum	1-10
118	35 8	Normal pelvis	890
166	43 5	Cervical erosion	1-40
4	Amenorrhea	Posthysterectomy—one ovary removed for cysts	1500
00	33 5	Parametrial tenderness	1500
86	26 3	Complete retroversion partial prolapse	1530
59	24 1	Complete retroversion	Traces
Average			1450

*Average does not include case number 59

Fig 3 SC6586 Edema of the endometrium on the fifteenth day of the cycle in a patient with retroversion of the uterus and pain and swelling of the breasts.

Fig 4 SC7059 Edema and hyperemia of the endometrium on the twenty first day of the cycle in a case with partial prolapse of the uterus and premenstrual breast pain.

ried woman of 24 with 1 child 8 years of age Menstruation had formerly been of the type 28,4, average, with slight discomfort but for 6 months the periods had been recurring at 5 to 7 week intervals and lasting but 1 day For 3 years the patient had been under treatment for pelvic inflammatory disease and during this time there had been a bilateral milky secretion from the nipples and premenstrual pain and swelling of the breasts She began to menstruate on the day of the operation after a 53 day interval

The pathology found at operation was as follows chronic salpingitis with adenomyosis of the uterine cornua endometriosis and papillomas of the ovary follicle and corpus luteum cysts of the ovary (Fig 1) The right ovary measured 4 by 4 by 4 centimeters and contained multiple cysts with small fibrous papillomas The left ovary was small and adherent and measured 1 by 1 5 by 0 5 centimeters A cyst in the right ovary containing 8 0 cubic centimeters of clear fluid, had a hormone content of only 2 6 mouse units

The nipple secretion, irregularity of menstruation, and pelvic discomfort were only partly relieved by the operation In spite of the removal of both tubes and the right ovary Eight months after the operation, the left ovary previously noted as atrophic had enlarged to nearly 2 inches in diameter

The ovary with multiple small cysts was, however a much commoner finding than the larger cysts of the type just described, particularly in cases with breast pain and diminishing menstruation. This ovarian condition, often termed "cystic degeneration," cannot at present be accepted as either the result or the cause of any known endocrine disorder The cyst lining is usually composed of small inactive appearing cells and the hormone content of the cyst fluid is apparently low The cystic ovary itself is often small and fibrotic and might as a rule be well under normal size were it not for the bulk of the cysts. The association of the cystic ovary with inflammation (Witherspoon) or congestion (Moench) was evident in a number of the present cases

Four cases in which cystic ovaries had been reported at operation were studied and no hormone abnormalities noted (Table IX C) In 1 of these patients a palpable cystic ovary was present during the period of the tests, the curve of her estrin excretion being shown in Graph 4 and the history of her case being given below

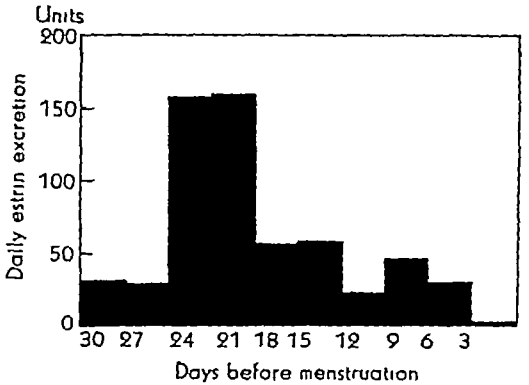
CASE 6 A. J First examination January 13, 1932 Patient was a married woman of 29, with 1 child 6 years of age Menstruation had always been of the 28 day type, formerly of 7 but now of 4 days duration and decreasing somewhat in amount, without dysmenorrhea The breast symptoms dated from a pelvic operation performed 3 years before admission, when the right tube and ovary and part of the left ovary were removed for multiple follicle cysts Since that time there had been a regular 2 day bilateral premenstrual pain in the breasts with a diffuse soreness over the entire surface of the anterior chest In addition there had been pain in the left leg, pain in the left abdomen, a mass in the left pelvis, dyspareunia, nervousness, frigidity, and epigastric distress

Examination showed the breasts small, dependent and slightly nodular The fundus was of normal size and in midposition, and the cervix eroded with endocervicitis In the region of the left ovary was a mass 5 inches in diameter, readily palpable above the symphysis The patient remained under observation for 2½ years with examination of the pelvis every 4 months The size of the cyst rapidly diminished after the first examination until only 1½ inches in diameter, but enlarged again to nearly its former size in June, 1933 After that, several fluctuations in size occurred The local pelvic symptoms and the indigestion were worse when the cyst was the largest, but no correlation between the severity of the breast symptoms and the size of the cyst was evident

The hormone tests for estrin and prolan in the blood and urine performed during a month of severe breast symptoms but with the cyst relatively small disclosed no significant abnormalities

In 5 cases the fluid of the ovarian cysts was assayed for its estrin content In 1 there was no hormone and in 3 only small quantities The fifth case with profuse nipple secretion was found to have a cystic corpus luteum which yielded 20 mouse units from its 8 cubic centimeters of fluid content In contrast with these 5, the follicle cyst in a patient with a typical case of endometrial hyperplasia (Fig 2) without breast changes yielded 90 mouse units

5 *The endometrium in cases of chronic mastitis* In 31 cases, sections of endometrium were available for study The 23 sections from cases with pain were normal except for 3, 2 of which showed a suggestion of glandular hyperplasia and 1 a carcinoma of the corpus The 2 sections of endometrium from cases with hypertrophy of the breast and the 6 from cases with secretion were all normal In the 20 cases in which the phase of the cycle at which the curettage was performed was on



Graph 4 Total estrin excretion in the 30 day cycle of a patient with painful breasts and cystic ovary Exp 57 Total units 1,741

record, the endometrium showed the expected morphology

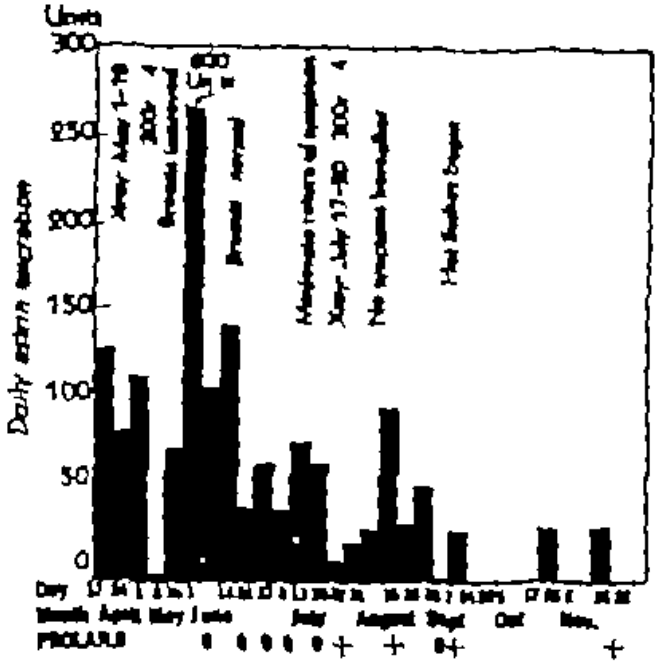
These results are important for, if chronic mastitis were due to a persistent hyperactivity of the ovary, one would expect a more or less constant association of the breast disease with endometrial hyperplasia Actually, the clinical aspects, particularly the age of the patients and the menstrual patterns, are quite dissimilar Only in elderly women with granulosa cell tumors have breast effects been reported in association with endometrial hyperplasia (Habbe, Muellerheim)

6 *Tests for the follicle hormone* It has been noted that Frank (15) found that the normal monthly excretion of estrin in the urine varied from 800 to 1,500 mouse units, and Siebke (51) from 200 to 2,000 The five determinations made on normal women in this study showed a wider range, namely, 760 to 3,150 units

The total monthly excretion of estrin was studied in 7 cases with pain and nodularity of the breasts, having various types of menstrual cycle and various pelvic lesions (Table IX B). The monthly rates varied from 600 to 2,930 mouse units, the average being 1,335

The excretion of estrin was similarly studied over a month's period in 6 cases of breast hypertrophy (Table IX C) The monthly rates varied from 740 to 3,900 mouse units, the average being 2,230

The monthly excretion in 6 cases with secretion from the nipple varied from 890 to 1,740 mouse units, the average being 1,480



Graph 5 Estimations of 24 hour estrin excretion at weekly intervals following radiation of the ovaries. Exp 47 24 hour specimens

(Table IX D) In the seventh case studied during a course of deep X ray therapy to the breast, there was an almost complete absence of hormone.

On account of the greater length of the menstrual cycles in the secretion group a perhaps better contrast is obtained by noting the average daily excretion. This, for normal women, had been found to be 56 mouse units. For the three different types of breast disease the average daily output was as follows hypertrophy 76 units painful nodularity 50 units secretion 42 units. Although these averages are based on the assay of 232 specimens, it cannot be maintained that the differences are significant.

The estrin of the blood was studied by weekly tests by the technique of Frank and Goldberger (17) in 19 cases The presence of the hormone was demonstrable at least once in 1 of 4 cases with pain 7 of 9 cases with hypertrophy and 3 of 5 cases with secretion.

7 *Tests for the presence of prolan* The prolan in the urine was studied by the examination of a total of 171 specimens from 14 cases, 4 with pain 4 with hypertrophy and 6 with secretion. Variable methods of extraction and high degrees of concentration, in some cases to show as little as 5 to 20 units per liter failed to give positive vaginal reactions. Minor changes in the ovarian follicles were noted when the higher concentrations were used, but these were decidedly less marked and less frequent than those commonly obtained from women in the menopause. Only in 3 cases with nipple secretion associated with delayed menses were there slight indications of an increase in prolan excretion

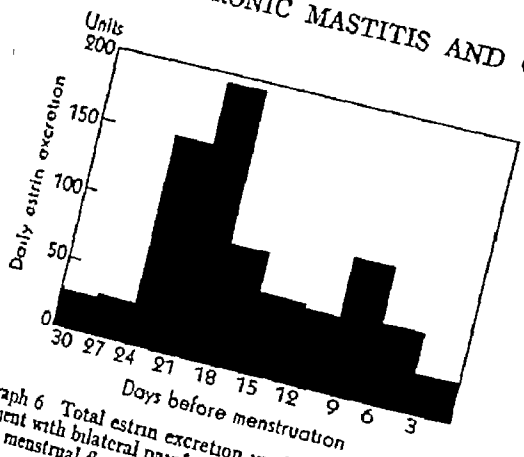
The presence of prolan in the blood serum was sought by weekly tests, using the Fluhmann (11) technique in 14 cases, 6 with pain, 4 with hypertrophy and 3 with secretion Some evidence of follicular ripening was apparently attained from several cases but in none was prolan definitely shown through the production of vaginal signs of estrus.

8 *The effects of radiation of the ovaries.* In 12 cases the effect of pelvic X ray and in 3 of radium from the uterus upon the clinical state of the breast was studied. In all but 1 there was immediate evidence of improvement in the pain and swelling and the nodularity of the breast tissue. In 6 cases in which the radiation dosage was sufficient completely to suppress the ovarian function, the improvement was permanent, whereas in 8 in which smaller doses were given there was a later partial return of symptoms.

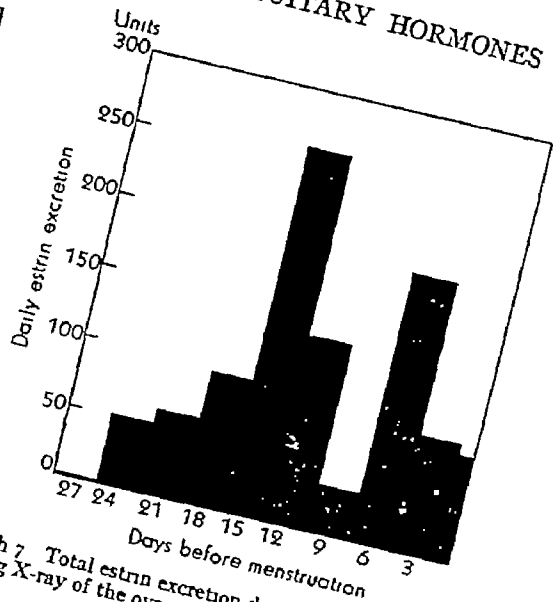
In 2 cases in which X ray of the pelvis was given the hormone excretion was studied for 3 months after treatment by weekly examination of specimens. In both, the improvement in the breast symptoms corresponded with a decided drop in the rate of estrin excretion and by the appearance of prolan in the urine

The effect of X-ray on the ovaries is illustrated in the following case.

CASE 7 R L was admitted to the hospital November 8, 1932 She was a married woman of 47 with 3 children, the youngest aged 7 years Tenderness and diffuse nodularity of the breasts and a little oily secretion from one nipple had developed 6 months before admission or 1½ years after a supravaginal hysterectomy for fibroids. Following four treatments, each of 300 r units, to the pelvis, there was a marked improvement in breast symptoms Two and a half months after the first series a second with the same dosage was given on account of a moderate return of the breast discomfort. Following the second series, the breast symptoms subsided entirely prolan appeared in the urine and only traces of estrin were excreted (Graph 5)



Graph 6 Total estrin excretion in the 30 day cycle of a patient with bilateral painful hypertrophy of the breasts and a menstrual flow of 1½ days Exp 44 Total units 2,300



Graph 7 Total estrin excretion during the 28 day cycle following X-ray of the ovaries Exp 66 Total units 2,830

In 2 cases an entire month's excretion of hormones was studied both before and after radiation of the pelvis The improvement in breast symptoms was again correlated with a great decrease in estrin excretion The history of 1 of these cases is as follows

CASE 8 R K, was admitted to the hospital October 1, 1931 She was 33 years of age, married but sterile Menstruation had formerly been of the type, 28,4, average, with occasional dysmenorrhea, until 4 years ago, when she was operated upon for a uterine fibroid and cystic ovary Following the operation the periods became reduced to 1½ days, while the breasts enlarged and developed a severe premenstrual tenderness.

During the month from April 4, to May 3, 1933, the patient's urine was collected and found to contain a total of 2,300 mice units of estrin (Graph 6) The blood tests for estrin (Frank and Goldberger) yielded positive reactions in the first and third week No prolan was demonstrable in 10 urine specimens by the alcohol precipitation method or in 4 specimens of serum.

From June 5 to 8, the patient received 4 X-ray treatments to the pelvis of 200 r units each

From June 6 to July 3, the patient excreted 2,830 mice units and had her usual menstrual period preceded by slightly reduced breast discomfort (Graph 7) Thereafter all breast symptoms rapidly subsided and no further period occurred for 11 months

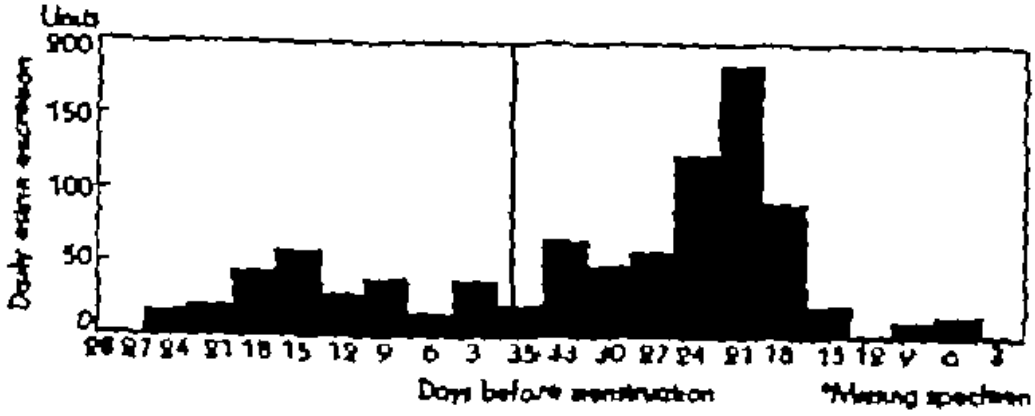
From August 29 to September 28, the estrin excretion was studied for a third time Only traces of estrin were discovered, the total amounting to perhaps 50 units for the month With the return of menstruation on June 27, 1934 there was a slight recurrence of the breast tenderness

The effect of radiation of the ovaries on the secretion of milk was less definite In 2 cases the disappearance of the discharge required 3 to 4 months and in one instance milk continued to appear for 5 years after a single high voltage treatment to the pelvis in an amount to produce erythema of the skin

Roentgenographs of the sella turcica in 3 cases of abnormal milk secretion failed to demonstrate any pituitary hypertrophy, and radiation of the pituitary by high voltage X-ray in one case failed to affect the symptoms

9 The effect of treatment with ovarian hormones Improvement in the painful breast following the use of ovarian extracts has been claimed (Cutler, Lerche, Whitehouse) The fact that these results have been observed even after the administration of tablets of the dried gland, containing what now must be regarded as negligible quantities of hormone, indicates that the improvement noted was not due to the specific therapy Treatment of either the painful or the secreting breast at the Memorial Hospital by the injections of potent preparations of the ovary or anterior pituitary has not produced constant effects

In the oophorectomized woman the administration of the ovarian hormones has led to swelling of the previously atrophied breast and to some painful sensations (Werner and Collier, Loeser) On the other hand, the ad-



Graph 8 Total estrin excretion of two cycles, showing increased output during administration of hormone in a patient with bilateral painful hypertrophy of the breast Exp 34. Total units first cycle, 740, second cycle 2,185

muniatration to menstruating women with chronic mastitis of even very large quantities of hormone, sufficient to produce a demonstrable rise in the rate of estrin excretion, has not caused in our experience any increase in the breast symptoms. The following case is illustrative

CASE 9 A P Patient was admitted to the Roosevelt Hospital, February 10, 1934. She was a woman of 25 with a history of encephalitis lethargica at the age of 15 and of one miscarriage 8 years before admission A *year after the miscarriage, a pelvic* operation had been performed for salpingitis and a cystic ovary Menstruation until the miscarriage had been of the type 28,3 average without pelvic or breast pain, but since then the periods had become totally irregular, very scant, and preceded by 2 weeks of pain, swelling and the development of lumps in the breasts The breasts had grown progressively larger and before the periods developed petechial hemorrhages in the skin above and within the areola

The patient was admitted to the gynecological ward of the Roosevelt Hospital on February 10, 1934 She was observed for 12 days before her period during which time her suffering was intense enough *to require the regular administration of codeine* The hemorrhagic spots appeared 5 days before her period and are shown in Figure 12 of Part I

During the 28 day cycle beginning February 22 1934, no treatment was given beyond rest in bed, support of the breasts, and sedatives Biopsies were taken on March 8 and March 22 14 days before and 2 hours after the onset of menstruation, respectively (Figs 13 14, of Part I) There was definite improvement in the breast symptoms during this month which could only be attributed to the physical and mental rest afforded by the stay in the hospital

Hormone tests The excretion of estrin during this month totaled 740 mouse units (Graph 8) There were four negative blood reactions (Frank and Goldberger) the last coinciding with a weakly positive Fluhmann test for serum estrin. There was no evidence of an increase in prolan in five specimens of blood serum or in ten urine specimens extracted by the tungstic acid method.

The patient s next cycle lasted 34 days, only 14 of which she spent in the hospital During this time she received a total of 132,000 mouse units of a commercial preparation of estrin in oil. The subsequent period was associated with a greatly reduced pelvic and breast discomfort and there were no hemorrhagic spots The urinary excretion of estrin rose to over 2 185 units, the patient failing to submit two of her specimens (Graph 8)

10 *Evidence of an associated pelvic congestion or parametritis* Reasons have been given in the first sections of the paper why a lesion of the pelvis having an effect upon the breast by way of the nervous system must be given consideration. Much of the data already discussed including the variations in the menstrual flow and the fibrotic or multicystic ovary might be interpreted either as evidence for a glandular or neurovascular disturbance The conditions to be discussed under the present head (Table X) have all been described by one or more previous writers as the causes of pelvic congestion or parametritis and each has also been previously reported in association with breast symptoms. The evaluation of their importance is concededly difficult since the conditions are such that *instances of each would be found in the examination* of any large series of women. Certain special characteristics of these conditions as they occur in the present series, their high incidence and the frequent simultaneous appearance and disappearance of breast and

pelvic symptoms, are points in favor of a more than accidental association

a An existent or previous history of pelvic inflammation was noted in a total of 27 cases These represented 12 5 per cent, 3 2 per cent, and 6 4 per cent of the cases with pain, hypertrophy, and secretion, respectively A striking feature of these cases was that many appeared not to have been of gonorrheal origin but to have followed an abortion The following case is illustrative

CASE 10 G S, was admitted to the hospital August 29, 1933 She was a married woman of 23, by occupation a night club hostess Five years before admission she had suffered a severe pelvic infection following an abortion For a year after that she was treated for pelvic inflammation and then operated upon Both tubes, which were adherent and acutely inflamed, were removed

During the last 5 years the patient's periods had been preceded by 10 days of marked pain and swelling of the breasts Menstruation was, however, irregular occurring every 2 to 4 weeks and lasting from 3 to 7 days Additional symptoms were diffuse premenstrual pelvic pain, abdominal distention, indigestion, leucorrhea, and dyspareunia Examination showed the breasts of medium size, dependent, nodular in the outer quadrants and exceptionally tender The uterine fundus was forward and fixed with attempted motion causing severe pain The ovaries were a little swollen and very tender The cervix was moderately eroded and discharging profusely

Hormone tests showed a 31 day excretion of 1,055 units of estrin with four negative blood specimens There was no evidence of an increase in prolan in 4 specimens of serum tested by the Fluhmann method or in 10 urines extracted by the tungstic acid method

The patient was treated for a year in the gynecological clinic, at the end of which time both breasts and pelvic symptoms were greatly improved

b Cases of typical "chronic parametritis" Besides these cases there were 62 others with various types of pelvic pain and uterosacral or broad ligament tenderness which appeared to correspond closely to the condition, described by Freund, as parametritis and with which he noted painful nodules in the breasts These represented 26 2 per cent of the group with breast pain, 16 1 per cent with hypertrophy, and 17 0 per cent with secretion The following case is a good example

CASE 11 R. S First examination was made September 26, 1933 Patient was 30 years of age, married for 12 months, but unable to conceive Menstruation before marriage had been of the type, 28,4, average, with moderate pelvic discomfort and a slight premenstrual swelling of the breasts Since marriage menstruation had been every 4 weeks lasting 4 days, with very severe lower abdominal discomfort In addition the patient suffered from constant backache, lower abdominal pain, discomfort on sitting down, dysuria, and dyspareunia to the extent of making coitus practically impossible During this same period of 12 months the premenstrual breast pain and swelling had greatly increased and there had been a permanent enlargement of the breasts to the extent of increasing the circumference of the chest, as measured by necessary changes in the brassière, 3 inches

Examination The breasts were medium in size, pendulous, with a moderate amount of nodular, glandular tissue in the outer quadrants The uterine fundus was normal in size and position but an extraordinary degree of tenderness was elicited on its attempted motion The cervix was without erosion but secreting great quantities of clear mucus The thyroid was a trifle enlarged

The patient was observed at intervals for a year The pelvic symptoms for which she primarily sought relief were always worse for several days after sexual intercourse and during 1 month that she spent by herself in the country she was largely free from both breast and pelvic complaints In spite of numerous relapses, the tendency was toward improvement and at the time of writing she is nearly symptom free and 3 months' pregnant

TABLE X —PELVIC LESIONS FOUND IN PATIENTS WITH BREAST DISEASE

	Cases with pain Per cent	Cases with hypertrophy Per cent	Cases with secretion Per cent
Pelvic inflammation	12 5	3 2	6 4
Parametritis	26 2	16 1	17 0
Retroversion	36 6	10 0	44 0
Endocervicitis	45 2	22 6	48 9

The clinical course and the subsequent pregnancy indicate that this in spite of the severity of the symptoms was a process quite distinct from the usual infectious salpingitis An example of a perhaps later stage of the disease with decreasing menstruation has already been described in Case 2

c Retroversion of second or third degree or partial prolapse of the uterus was noted in 91 cases These represented 36 6 per cent, 10 0 per cent, and 44 6 per cent of the cases with pain, hypertrophy and secretion, respectively

The relation of uterine malposition to breast disease may appear remote. Nevertheless there are three articles in the literature reporting the cure or improvement of mammary pain by the reposition of a misplaced uterus (Ayler Hastrup Miller) It is known furthermore that a uterus in retroversion or partial prolapse may affect the pelvic circulation to the extent of producing broad ligament varices and possibly many secondary changes. In the present series, there were 14 cases with retroversion and breast disease in which the pelvis was observed by the writer at the time of celiotomy The uterus in these cases was regularly found swollen and congested. Histological evidence suggesting a vascular disorder in the pelvis is found in a few cases with exceptional edema and hyperemia of the endometrium and ovary (Figs. 3 4) That this general pelvic hyperemia may affect both the ovaries and the autonomic nerves of the pelvis must be admitted.

d. Endocervicitis erosion or infected laceration were noted in 114 cases representing 45.2 per cent 22 6 per cent, and 48.9 per cent of the 3 groups of cases. These are minimum figures for among those counted as normal are 27 cases not examined and 56 cases incomplete to the extent of their being no record of the condition of the cervix.

The group with cervical disease has been placed in the pelvic congestion group for two reasons First, a hypersecretion of the cervical glands is probably often the result of pelvic hyperemia and may be its only symptom. On the other hand parametral infection may arise through the lymphatics from a diseased cervix. In the literature are also to be found numerous reports of hypertrophied and infected cervices in association with breast disease and the cure of the latter after treatment or amputation of the cervix (Aitken, Roeth, Copland Miller)

e A relationship between certain breast conditions and disorders of the sexual function has been described repeatedly in the literature (Rosenthal Glass, Samuel, Witthauer Rulz Dickinson) No complete statistical survey of this aspect could be made in this series, but a few points are noteworthy In 22 patients the symptoms developed at the time of marriage. Twenty three women complained of dyspareunia. Of 76 women questioned the majority were practicing contraception by methods which were possible causes of pelvic congestion. The relationship between a sexual difficulty and the development of physical changes in the breast is well illustrated in the following case

CASE 12. N D Patient was admitted to hospital October 7 1931 She was 28 years of age, married for 1 year without pregnancies Six months after marriage the patient had first noted premenstrual pain, swelling, and the appearance of lumps in the breasts. Examination showed the breasts medium in size and dependent with an extraordinary diffusely swollen appearance, dilated veins on the surface, and large, partly circumscribed areas of induration in both outer quadrants. The pelvis was normal except for a hypersecretion of the cervix.

At the patient s second visit she volunteered a long story of psychological difficulties in childhood, resulting she believed in a complete inability to adapt herself to normal marital relations. Temporary separation from her husband was under consideration. Two months later the patient reported by letter that she had adopted this course and that her breast trouble had completely disappeared.

f The time of appearance of breast symptoms In 92 cases the onset of breast symptoms was traceable to a definite incident in the patient s life which furnished a reasonable cause for the development of a pelvic congestion or parametritis. Thus the symptoms began at marriage in 25 after abortion in 12 after childbirth in 22 following pelvic operation in 26 and coincident with pelvic inflammation in 7 In 34 cases a pelvic condition of this type was suggested by the beginning of a secondary dysmenorrhea at or near the time of onset of the breast symptoms (Table XI)

11 Dysmenorrhea and breast symptoms Primary dysmenorrhea was present in 52 per cent of the 50 unmarried women of the series, representing 55 5 per cent of the 36 cases with pain, 60 per cent of the 10 cases with hypertrophy but none of the 4 cases with secretion This symptom occurring with breast pain is subject to various interpretations, for on the one hand dysmenorrhea has been attributed to an increased contractility of the uterine musculature from follicular hormone stimulation (Kraus, Reynolds, Novak) and on the other it has been successfully treated by sac

tion of the presacral nerve (Cotte, Counseller and Craig)

12 The association of thyroid disorder with breast disease The coincidence of thyroid disorder and various types of pelvic disorder is well known There may be, as is the case with the breast, a premenstrual thyroid enlargement as well as an apparent relationship to various menstrual anomalies, certain pelvic lesions and possibly sexual activity In the present series there were noted 21 cases with definite thyroid enlargement and minor degrees of fullness were quite common, especially among the younger women In 5 cases, 4 with pain and 1 with hypertrophy of the breasts, the thyroid abnormality was the only criterion for the classification of the case The treatment of 2 cases by irradiation of the thyroid was followed by subjective improvement in the breast condition

13 Psychic factor in breast disease Repeated reference has been made in the literature to the excitable temperament of patients with the painful breast and the development of symptoms at times of nervous stress Taylor) Corroboration of this was found in many instances in the present series in which symptoms were made worse during periods of anxiety resulting from economic worries, the illness of relatives or marital difficulties Pelvic symptoms from similar causes have been reported (Meyer-Ruegg) The following case illustrates the rapidity with which the breast, presumably through its vascular system, may in predisposed individuals respond to trivial psychic stimuli

CASE 13 D T, was admitted to hospital March 15, 1933 She was unmarried, aged 18 Menstruation, which had begun at 13, was slightly irregular, of the 21–28 day type, lasting 6 days and associated with backache, headache, abdominal pain, and cramps so severe as to cause confinement to bed

The breasts began to develop at the age of 12 and have continued to grow For 10 days each month there was a premenstrual swelling with severe pain radiating down each arm In addition the patient reported that throughout the month she frequently experienced abrupt swelling of the breasts with any excitement such as a trivial accident at the dinner table, an unexpected visitor, or an anticipated social event

Examination showed a slender white girl with enormous pendulous breasts, out of all proportion to her age and size The breast tissue was diffusely nodular throughout, the nipples normal, the areolæ wide and dark Rectal examination revealed a small, anteflexed uterus The thyroid was slightly and symmetrically enlarged The urine estrin excretion was normal but the blood test gave a positive reaction in the specimens of both the first and third week

TABLE XI —INCIDENTS ASSOCIATED WITH THE ONSET OF BREAST SYMPTOMS

	Cases with pain	Cases with hypertrophy	Cases with secretion	Total
Marriage	17	7	1	25
Abortion	10	0	2	12
Childbirth	16	0	6	22
Pelvic inflammation	6	1	0	7
Gynecological operation	13	7	6	26
Menstrual change	50	13	19	82
Onset of dysmenorrhea	26	3	5	34

DISCUSSION AND CONCLUSIONS

The general conclusion of this study is that a certain minimum activity of the ovary is necessary for the development of chronic mastitis but that no specific hyperfunction or hypofunction of the ovary is at present demonstrable This result is contrary to hopes entertained at the beginning of the work and contrary to what might have been expected from the known proliferative effects of the ovarian hormone on the breast tissue

Certain exceptions and reservations must be made In one small group of cases in which swelling of the breast, sometimes with secretion, develops in the presence of a persistent follicle or corpus luteum cyst, a hormone cause is probable, but the clinical aspects of this condition are different from that of the common type of chronic mastitis with painful outer quadrant induration It is not unlikely that other unrecognized reactions of the breast to certain hormone states may exist

Even for the common type of mastitis, however, it must be conceded that the present method of study has not exhausted the possibilities of a hormone cause Present technical methods for the clinical determinations of estrin and prolan are far from perfect and no satisfactory test exists for the quantitative

study of the corpus luteum hormone in body fluids. A very slight disturbance of gland function might cause hyperplasia in the breast when active over a considerable number of years and yet not be obvious when studied by relatively crude laboratory methods over a month's time. Irregularities in the peaks of production or excretion of estrin may furthermore have a significance quite aside from the total quantities chiefly discussed in this paper. Finally it is possible that the abnormal estrin effects on the breasts may be the result of local conditions such as an increased responsiveness to normal quantities of hormone possibly as the result of local hyperemia or a tissue concentration of the gland substances, bearing no relation either to the actual activity of the ovary or to the amount of hormone in the blood stream.

With these reservations, the following summary is offered of the present knowledge of the conditions under which chronic mastitis is found to develop.

A. THE PAINFUL NODULAR BREAST

1 An active ovary producing estrin must be present

a. The painful breast is limited to women before the menopause and after puberty.

b. The pain and nodularity improve with X-ray and surgical castration, such improvement paralleling the fall in estrin excretion in the urine.

2 There is no indication of an extensive ovarian activity

a. The histological structure of the painful breast does not show the uniform epithelial proliferation of a hormone produced hyperplasia.

b. The 7 cases studied did not contain any excess of estrin in the urine or blood and in several cases the estrin excretion was quite low.

c. The endometrium in cases of the painful breast does not show the hyperplasia to be expected with hyperactivity of the ovarian follicle.

d. Administration of considerable quantities of ovarian hormone to patients with the painful breast does not increase the severity of the symptoms.

3 There is no indication of an underfunction of the ovary

a. The average excretion of estrin in 7 cases which were studied was within normal limits and in several of these cases rather high values were found.

b. The scant menstruation noted in 16.9 per cent of the women with the painful breast was the chief evidence for the underfunction theory but the estimation of the estrin excretion in such cases gave normal values.

c. Consistent results have not been obtained in this clinic by the treatment of the painful breast with estrin or the ovary stimulating hormone of the anterior pituitary.

4 A "dysfunction" of the ovary remains a possibility which cannot be entirely excluded

a. Delayed or irregular menstruation, which must be accepted as a sign of a disturbed ovarian function was present in 13.7 per cent of the cases.

b. Irregularities in the curves of estrin excretion or of blood concentration may eventually be shown to have some significance but knowledge for their interpretation is at present lacking.

c. The multicystic ovaries observed in so many cases also may be taken as evidence of a disturbed ovarian function but they may be looked upon as well as the result of vascular congestion in the pelvis.

5 A corpus luteum disorder cannot be excluded since tests do not exist for studying the blood and urinary levels of this hormone

a. The frequency of normal menstrual rhythm, the histological evidence of a regular endometrial cycle and the rarity of evident disease of the corpus luteum in patients operated upon are evidence against this factor.

6 There is no indication of a hyperactivity of the anterior pituitary

a. Prolan appears in the urine only in cases of pronounced underfunction of the ovary which is never found with the painful breast.

b. An increase in prolan in the urine comparable with that taking place in the menopause has been excluded by the present series of studies.

c. The appearance of prolan in the urine after X-ray of the ovaries occurs at the time of improvement of breast symptoms.

7 *The painful breast has from the clinical viewpoint a large nervous element*

a The pain and tenderness are more marked than are to be expected in an endocrine produced glandular hypertrophy

b The pain radiates to the arm, neck, axilla and lateral body wall and may be associated with hyperesthesia of the skin of the whole thorax

c The pain and swelling in certain cases are produced or become worse during periods of nervous tension and may even develop abruptly within a few minutes after a nervous shock at any time in the monthly cycle

d Various associated nervous complaints are described by the patient including insomnia, anxiety, palpitation blurring of the vision, mucous colitis and headaches

e One case report exists in the literature of the disappearance of the premenstrual breast symptoms in one breast after the destruction of the thoracic sympathetic of that side

8 *A local state of vascular congestion is a prominent feature of the painful breast*

a The gross appearance of the painful breast before menstruation with its hyperemia of the areola venous dilatation and increased weight alone suggests hyperemia

b The histological signs of this vascularity may be demonstrated in the "edema" of the lobule

c The relief afforded by the onset of menstruation is usually too rapid to be explained as the result of epithelial regression

d The sudden appearance of pain and swelling in the middle of the cycle in certain cases cannot be ascribed to epithelial proliferation

e Simple support of the breast often causes considerable amelioration of symptoms

f In one case described with pain and hypertrophy, petechial hemorrhages occurred regularly before menstruation in the skin about the areola

9 *The coincident gynecological lesions and menstrual disturbances have a possible significance as evidence of an associated vascular congestion and tissue edema in the pelvis*

a The common pelvic lesions are classifiable as adnexal inflammation, parametritis, retroversion, and cervical infection

b The onset of pelvic symptoms and breast pain after marriage, abortion, or pelvic infections is significant of parametrial congestion or inflammation

c The scant menstruation may be regarded as the effect of the secondary fibrosis in the pelvis described by many writers as the end-result of chronic pelvic congestion

d The edematous cystic, and fibrotic ovaries may have a similar cause

One may offer the following provisional conclusions on the cause and nature of the painful diffusely nodular type of mastitis as follows

1 The ovarian hormone is certainly a necessary factor, but it has not been possible by present laboratory methods to demonstrate any specific abnormality of ovarian or anterior pituitary function It is, however possible that refinements in technical methods may eventually reveal a definite endocrine disturbance

2 The conception of the disease as primarily a vascular disturbance with changes occurring in the interstitial tissues of the breast based on abnormal nervous stimuli explains many of the clinical aspects of the disease Such a view can only be accepted with caution, however, because it requires the assumption of a physiologic mechanism yet largely undemonstrated

B BREAST HYPERTROPHY OCCURS IN AT LEAST TWO FORMS

1 In one group in which there is a simple painless enlargement of the breasts of relatively uniform consistence an endocrine factor is clearly prominent This includes the hypertrophy developing in childhood and in old women in the presence of the specific ovarian neoplasms, such as the granulosa cell tumors and teratomas Breast swelling has also been observed in the presence of persistent corpus luteum and follicle cysts and ascribed to a polyhormonal amenorrhea Breast hypertrophy after hysterectomy may, in some cases, have a similar basis

2 The painful hypertrophies of this study were not of this type and resembled closely the tender nodular breasts, both in regard to their physical characteristics and the condi-

tions under which they occurred. Hormone studies of a series of these cases gave normal blood estrin values, rates of monthly excretion of estrin a little higher than in the cases of the painful breast, but still probably within normal limits, and no increase in prolan excretion. X ray of the ovaries led to a disappearance of the pain and to a reduction in the size of the breasts but the use of ovarian hormone by mouth or hypodermic was ineffectual. The coincident pelvic lesions and the incidents associated with the onset of the breast enlargement were in general the same as those found for the painful breast.

The conclusions in regard to the causes of this type of hypertrophy must be similar to those for the painful, nodular breast.

C. ABNORMAL SECRETION FROM THE NIPPLE

The local physical characteristics as well as the conditions under which abnormal nipple secretion occurs seems to distinguish it somewhat from the two preceding groups. the average age of these patients was higher. the proportion of women with preceding pregnancies was much greater. menstrual disturbances were more frequent, particularly in the form of delayed menstruation. the average daily excretion of estrin was lower. the secretion did not disappear at once after X-ray of the ovaries.

In many cases, however the characteristics of the painful breast were present notably the cyclical pain and swelling. the diffuse nodularity and certain coincident pelvic lesions.

It is concluded that the cases with abnormal secretion are a heterogeneous group. the following representing a possible classification of these.

1. Cases with a non-specific discharge, serous, sanguineous or purulent, from local disease of the larger ducts.

2. Cases reported in the literature with a definite nervous factor either in the form of direct stimulation of the nipple or a central nervous system disease, such as tabes dorsalis or syringomyelia.

3. Cases reported in the literature with definite evidence of endocrine disease, such as the instances of amenorrhea with follicle or corpus luteum cysts. To this group may be long the cases of temporary secretion in the early menopause, theoretically ascribable to the sudden decrease in ovarian activity or the increased function of the anterior pituitary.

4. In a large group of cases one is forced to maintain the alternative theories noted for the other two types of breast disease, namely an as yet undetermined variety of endocrine disturbance or a little known form of neurovascular disorder.

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REPRODUCTIVE EFFICIENCY BEFORE AND AFTER THE BIRTH OF MALFORMED CHILDREN

A Study of 405 Consecutive Families

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THIS is the second report dealing with families in which malformed children have been born The first one concerned the place-in-family of the defective child (2)

The present communication deals with the remaining pregnancies in these families It concerns, primarily, those which did not terminate normally, and which may be classified as "disturbed," a "disturbed" pregnancy being defined as one which ended in either a miscarriage (including abortions), a stillbirth or a premature birth The chief interest of the study concerns the closeness of the disturbance to the defective child

If miscarriages, stillbirths, or premature births should take place closer to the defective child pregnancy than would be expected according to the laws of chance, it would suggest that both these disturbed pregnancies and the defective child pregnancy were but different expressions of a prolonged period of decreased reproductive power If this were so it would seem to lend weight to the hypothesis that congenital malformations are due to defects in the germ plasm taking place before the moment of fertilization Whereas if the disturbed pregnancies occur at random in the family, there would be less reason to believe that the reproductive power of the mother exhibited any prolonged period of weakness The present report attempts to elucidate this theoretical conception

Materials and methods To quote from the first communication "There were found in the files of the Bureau of Vital Statistics, Department of Health of the State of Pennsylvania, 130,132 death certificates for stillborn and liveborn individuals who died in Philadelphia during the 5 year period between January 1, 1929, and December 31 1933 Each of these certificates was examined and the data on those noting the existence of any congenital defect, were transcribed to duplicate, official forms Fourteen hundred and seventy-six such certificates were located

"The deceased individual was considered to have possessed a defect under either of two conditions (1) if the defect involved the surface of the body, or (2) if internal, its presence had been disclosed by operation or necropsy Diagnoses not conforming to these requirements were considered as not verified and were excluded from further consideration This procedure reduced the number of usable certificates to 890, or only 60 per cent of the original 1,476 certificates

"An attempt was made to interview the mother of each of the 890 deceased individuals, the visits being made in the summer of 1934 by 3 fourth year medical students A complete reproductive history was secured from each mother that could be located The group forms a consecutive series All of the defective children died within a given geographical area and within a given period of time"

In order to have a homogeneous group of reproductive records for analysis it was necessary to omit from consideration certain families forming the group of 539 families reported upon in the first paper Families in the above group, having the following characteristics were not used in the present analysis (a) Those with more than one defective child, (b) those families in which there was only a single conception, (c) families in which the mother was married twice and in which families the defective child was born to the second husband This procedure reduced the number of families from 539 to 405

RESULTS

Diagnosis of defective child In the 405 families there were 405 congenitally malformed children (Table I, column 2) The most frequently recurring chief diagnoses (column 1)

TABLE I—DIAGNOSIS OF CONGENITALLY MALFORMED CHILD

Diagnosis	Children					
	Total		Disturbed pregnancies		Undisturbed pregnancies	
	Number	Per cent	Number	Per cent	Number	Per cent
(1)	(2)	(3)	(4)	(5)	(6)	(7)
Reported	405	100	151	100	254	100
Hydrocephalus	98	24	29	19	67	26.4
Spina bifida	53	13	26	17	27	10.6
Anencephalus	48	11.9	17	11	31	12
Hydrocephalus, spina bifida	31	7.6	7	4	24	9.5
Pyloric stenosis	29	7		7.9		4.7
Heart disease	25	6	10	6.6	15	5.9
Monster	16		7	4.6	9	3.5
Intestinal obstructions	10	4	8	5.3	2	
Cryptorchidism	9		3		6	
Hare lip, cleft palate	8		3		5	2
Gastroschisis	8	1.5	3		5	
Macrocephalus	6	1	3		3	
Meningocele	4	1		1	3	2
Others	21	5	5	3.3	17	6.7

Showing in column 1 the chief diagnoses that occurred most frequently in the families which form the basis of the present report in column 2, the frequency with which the various defects were observed, in columns 4 and 6, the relative frequency of the defects as they appeared in families with and without any disturbed pregnancies Note that there was no essential difference in the frequency with which the different defects were observed in the two groups.

and the number of children in each group (column 2) are recorded in this table. Hydrocephalus was the most common defect spina bifida, with and without hydrocephalus, and anencephalus were the next most frequent diagnoses.

In the 405 families, 151 families, or 37.3 per cent had one or more disturbed pregnancies (Table I column 4) and 254, or 62.7 per cent, had no disturbed pregnancies (Table I column 6) These two groups can be compared in Table I with respect to the diagnoses of the malformed children in each There appears to be no essential difference in regard to the types of defects found in the two groups.

In the 405 families, there were 1,312 conceptions (Table II) Over 60 per cent terminated normally with live born fully developed offspring Twenty three per cent resulted in the birth of malformed infants and 13 per cent resulted in either miscarriage, stillbirth, or premature birth

The relative positions of the various disturbances of pregnancy in relation to the position of the conception which resulted in the birth of the congenitally malformed child are shown in Table III The position of the defective child pregnancy is indicated by the heavy face, horizontal line. The place-in-family of all other conceptions is shown in column 1 In this column, the place immediately preceding that which ended in the birth of the defective child is indicated by −1 the conception which followed immediately that of the defective child is indicated by +1 The conception preceding, and next but one to the defective child conception is indicated by −2 and the conception following, next but one to the defective child pregnancy is indicated by +2 and so on The observed frequencies of miscarriages, stillbirths, and premature births by birth position in relation to the position of the defective child are indicated separately in columns 2 3 and 4 Their observed combined frequencies are given in column 5 Their expected combined frequencies, had they been distributed by birth position according to the laws of chance are shown in column 6

The latter distribution was computed by the use of the Greenwood-Yule reconstruction (1) The method is as follows The expectancy that a characteristic occurring at random will take place in any particular position depends upon the size of the family For example, in a family of three siblings, in which there is one defective sibling, there is one-half a chance that each of the two remaining siblings will be affected, in a family of four siblings, in which one sibling is malformed, only one-third a chance exists that any one of the three remaining siblings will be affected

Using this method, the fractions contributed to each birth position by each family were totaled by birth position for the entire group of families In those in which there were two disturbed pregnancies, each position was allotted double the fractional value given to families with only one disturbed pregnancy In families with three disturbed pregnancies, each birth position was given triple the birth value given to those families with only one disturbed pregnancy, and so on, depending on the number of disturbed pregnancies in the family

Since all disturbed pregnancies in each family were counted in the total of column 5, and since in column 6, each family was counted once for each disturbance noted in column 5, the total of these two columns are necessarily approximately equal

The ratio of the observed, combined frequencies of the disturbed pregnancies (column 5) to their expected, combined frequencies (column 6) is shown in column 7 Had the observed disturbances occurred with random frequency in the various birth positions, the figures in each birth position in column 5 would have been, for all practical purposes, identical with those in column 6 This identity would have produced a ratio in column 7 of 1 0 for each birth position

The figures in column 7 show that the disturbed pregnancies in the position −1 and +1, immediately adjacent to the defective child, occurred more often than would be expected according to the laws of chance. In the birth position immediately preceding that of the defective child, the observed disturbances were the most frequent, being next most common in the position immediately following that of the defective child In the majority of the more distant positions, the disturbances occurred less often than would be expected by chance Three of the distant positions (−3, −6, −9) showed a greater frequency than would be expected by chance These values are believed to be false due to the fact that the number of families forming the total group was so small

TABLE II —MALFORMED OFFSPRING AND DISTURBED PREGNANCIES IN 405 FAMILIES

Conceptions	Conceptions	
	Number	Per cent
Total	1732	100 0
Terminating normally	1094	63 2
Ending with malformed offspring	405	23 4
Ending with miscarriage, stillbirth, or premature birth	233	13 4

Showing the number of conceptions experienced by 405 mothers, each having one malformed child, and the number of disturbed pregnancies among the remaining pregnancies Note that more than one-third of all of the pregnancies were abnormal

Considering the relative sizes of the observed frequencies in the −1 and −2 positions, column 5, it is evident that the frequency in the −1 position is approximately two and a half times that of the −2 position These figures refer to the combined miscarriages, stillbirths, and premature births If these combined disturbances of pregnancy are sub-grouped, as shown in columns 2, 3, and 4, the following is observed The frequency of miscarriages alone (column 2) in the −1 position is more than twice as great as in the −2 position, the frequency of stillbirths (column 3) in the −1 position is two and a half times as great as in the −2 position, and the frequency of premature births (column 4) in the −1 position is over three times as large as in the −2 position These individual observations lead one to conclude that the nearness of the miscarriages, the stillbirths, and the premature births to the position of the defective child were individually determined by a common cause, and by the same cause, which, in all probability, brought about the congenital malformations in the families in this group

TABLE III.—THE OBSERVED AND EXPECTED DISTURBANCES OF PREGNANCY

Conception place in family	Observed				Expected	Ratio
	Miscarriages	Stillbirths	Premature births	Combined miscarriages, stillbirths, premature births	Combined miscarriages, stillbirths, premature births	
	Number	Number	Number	Number	Number	
0	(1)	(2)	(3)	(4)	(5)	(6)
−[illegible]					[illegible]	[illegible]
−[illegible]					[illegible]	[illegible]
−10					[illegible]	[illegible]
−9	[illegible]		[illegible]	[illegible]	[illegible]	[illegible]
−8					[illegible]	
−7			[illegible]	[illegible]	[illegible]	
−6	[illegible]				[illegible]	
−5					[illegible]	[illegible]
−4	[illegible]	[illegible]			[illegible]	[illegible]
−3	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	
−2	[illegible]	[illegible]		[illegible]	[illegible]	[illegible]
−1	[illegible]	[illegible]		[illegible]	[illegible]	[illegible]
+1	[illegible]	[illegible]		[illegible]	[illegible]	[illegible]
+2	[illegible]	[illegible]			[illegible]	[illegible]
+3	[illegible]				[illegible]	[illegible]
+4					[illegible]	[illegible]
+5						[illegible]
+6					[illegible]	[illegible]
Totals	[illegible]	[illegible]	[illegible]		[illegible]	[illegible]

The heavy face horizontal line indicates the place in family of the congenitally malformed child. The minus numbers in column 1 represent the conceptions which preceded the defective child, plus numbers those which followed. The −1 position represents the conception immediately preceding, and +1 the one immediately following the defective child. The figures in columns 1, 2, and 3 represent the observed miscarriages, stillbirths and premature births, and in column 4 they are combined. The expected frequency of the combined miscarriages, stillbirths, and premature births in column 5, had they occurred at random, is shown in column 6. The ratio of the observed to the expected figures is shown in column 7.

On the basis that 0 is normal expectancy, the figures in column 7 show that the disturbances of pregnancy (column 4) occurred more often than expected in the positions close to the defective child, and less often in the more distant positions. The small number of families studied accounts for the ratios greater than [illegible] found in the −1, −6, and −9 positions.

RECAPITULATION

The above observations suggest that mothers who give birth to congenitally malformed individuals exhibit varying length periods of decreased reproductive efficiency. In most cases this period covers only the time required for the conception and birth of a single child. In other instances, the period is longer, and during this time, in addition to the conception and birth of the malformed child, other conceptions take place which do not end normally.

Since these disturbances of other pregnancies tend to cluster about the pregnancy which results in the birth of the congenitally malformed child, and because all of the disturbances and the malformations vary in character and degree one from the other, their multiplicity lends weight to the hypothesis that congenital malformations are due to defects in the germ plasm, rather than to forces which may operate upon the fertilized egg.

The finding of the disturbance so often in the pregnancy immediately preceding that which results in the deformed child suggests that the appearance of a disturbed pregnancy should make the obstetrician suspect the pos-

sible existence of a congenital malformation during the course of the succeeding pregnancy

SUMMARY AND CONCLUSIONS

1 The reproductive activity of 405 mothers, each having had a congenitally malformed child, is reported with respect to the incidence of miscarriages, stillbirths, and premature births

2 Of the 405 families, 151 or 37 3 per cent, exhibited one or more miscarriages, stillbirths, or premature births

3 Of the total of 1,732 conceptions in the 405 families, 63 2 per cent ended normally, 23 4 per cent resulted in malformed children and 13 4 per cent ended in either miscarriage stillbirth, or premature birth

4 Miscarriages, stillbirths, and premature births occurred more often than would be expected by chance in the pregnancies immediately preceding and immediately following the pregnancy which resulted in the birth of the defective child and less often than would be expected by chance in the remaining pregnancies Miscarriage, stillbirth and premature birth occurred most often in the pregnancy immediately preceding that of the defective child

5 From the above observations, it is concluded that the birth of a congenitally malformed child may be only one expression of a prolonged decrease in functional reproductive activity, the other expressions being miscarriages stillbirths, and premature births

6 It is suggested that the obstetrician has unusual reason to suspect the possible existence of a congenital malformation in the pregnancy which follows immediately after a miscarriage, a stillbirth, or a premature birth

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LOCAL ANESTHETICS PRODUCING PROLONGED ANALGESIA ELIMINATION OF PAIN AFTER RECTAL OPERATIONS

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THE most important unsolved problem in proctology today with the exception of a cure for cancer is the elimination of pain after rectal operations. This holds true because, if we cannot operate on patients without causing severe postoperative pain, we cannot operate on most of them at all. Most patients wish to avoid a rectal operation anyway and if there be also the knowledge that operation will be followed by hours of extreme suffering they will drag around with trouble for years rather than come for relief. Their apprehensions are not without basis. After the usual ligature operation for hemorrhoids, the routine orders of Miles are given ½ grain of morphine shortly after operation then tincture of opium every 4 hours for 24 hours, then every 6 hours for 24 hours, and then every 8 hours for the third and fourth days. An article just published on postoperative care by Best states that after all is done to relieve postoperative pain the patient is likely to need morphine and codeine. Patients who have received such doses of narcotics say that they feel dizzy but still suffer.

Rectal surgery becomes thoroughly satisfactory to all when after an operation under local nerve block, the patient can sit up in bed enjoy a good rest is free from pain, comfortable, and perfectly happy. That this can be approximated in the majority of patients will be shown.

Elimination of pain after rectal operations demands both an open type of operative technique, and also the use of anesthetic solutions having a prolonged local analgesic action for 3 days after operation. The factor of operative technique will be touched upon briefly later the main portion of this study is devoted to a new understanding of local anesthetics of prolonged action.

Of such anesthetics, some have been recommended so recently that their properties have not been understood. Some are dangerously toxic. Some are likely to cause undue tissue irritation or sloughing. Heretofore we have been left largely to guess work or to experiments on patients, without accurate laboratory measurements to know beforehand just what concentration of these solutions would or would not cause tissue injury. The purpose of this paper is to present measurements of the local irritation and of the duration of local anesthesia produced by various agents.

THE SOLUTIONS STUDIED

Quinine and urea dihydrochlorids. A practitioner in the rural districts of Arkansas (Thibault) in using quinine by hypodermic to treat malaria, discovered its prolonged local anesthetic properties, and popularized its use in the double salt of quinine and urea dihydrochloride.[1] This salt makes a strongly acid solution and although the official name has been quinine urea hydrochloride, the more accurate name is quinine urea dihydrochloride.

This preparation was abandoned by the general surgeons, who found that it caused induration, edema, and sometimes sloughing but it is still used by a number of excellent proctologists in rectal surgery where its irritant properties are less deleterious.[1] Arthur Crookall of Portland, Oregon, has used it in ½ per cent solution in 1,000 cases and states that in these it never caused a slough. He does not claim that in this weak concentration it entirely eliminated postoperative pain but he does claim that it lessens the pain. Finsterer used this same ½ per cent concentration in

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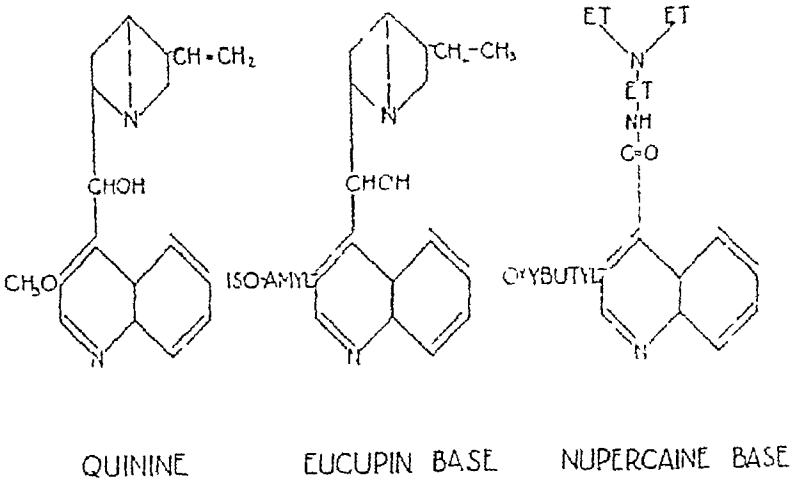

Fig 1 Eucupin, modification of quinine molecule

rectal surgery Saphir (56), of New York City, has used it in ½ to ¼ per cent solution in over 2,000 hemorrhoidectomies, and at first reported that in these low concentrations there were no sloughs More recently he has had sloughing even in the 0 5 per cent solution in water and has abandoned it (57) In stronger concentrations, usually 5 per cent, it has been used for injection under anal fissure by W O Green, A B Graham, Yeomans, Hirschman, E G Martin, and others[1] I shall show that it causes unnecessary pain on injection and unnecessary danger of sloughing, and that better solutions are available

Quinine hydrochloride with urethane So far as I know I am the first person to use this solution for local anesthesia While working with it in experiments on a different problem, I discovered by accident that not only was it less painful, but also less irritating and less likely to cause a slough than quinine urea dihydrochloride[2]

Eucupin By modifying and lengthening two side chains of the quinine molecule, the anesthetic potency to the rabbit's cornea may be raised 3,000 per cent eucupin (isoamylhydrocupreine) is one of these modifications (Fig 1) It was first synthesized as a bactericidal substance and found to be bactericidal to streptococcus in 1 4000 and to staphylococcus in 1 800 (45) (bacteriostatic to staphylococcus in 1 160,000) While using it in the eye, Morgenroth discovered its high potency as a local anesthetic Its prolonged action is explained by the fact that it remains in the tissues locally and may be recovered for analysis 4 days after it is injected (3)

Henius, in Germany, has used it in a 2 to 5 per cent ointment or suppository for relieving the pain of anal fissure It has also been applied in ⅓ to 2 per cent aqueous solution to ulcerating carcinoma both for its anesthetic action and also to clean up secondary infection

Vuzin (iso-octylhydrocupreine) belongs to the same hydrocupreine series as eucupin but has a longer side chain Lipschitz and Freund (34) found that it inhibited cell oxidation only half as much as eucupin and this suggested the likelihood that it might cause less local irritation than eucupin The hemolysis tests of Bijlsma and of Schmidt also suggested that it might be less irritating than eucupin Fromherz found that it effected a more prolonged anesthesia of the sciatic nerve of the frog than eucupin It was therefore included in the studies to follow

Nupercaine is something like a hybrid of quinine and procaine containing as it does the

[1] Martin now uses the quinine urea hydrochloride under anal fissure in 3 per cent after experiencing sloughing with the 5 per cent (57)

[2] This solution was first injected subcutaneously in the treatment of malaria. Pain was found to be less after its injection than after the injection of other quinine solutions (16) Later, because of its solubility, it was introduced by Genevrier in a highly concentrated solution for the injection treatment of varicose veins The supersaturated solution in water used for varicose veins must not be used for anesthesia

TABLE I.—MINIMAL LETHAL DOSES PER KILOGRAM BODY WEIGHT IN THE RABBIT AND COMPARATIVE AMOUNTS OF CLINICAL SOLUTIONS WHICH WOULD THEREFORE BE EXPECTED TO BE LETHAL TO A 70 KILOGRAM MAN

[illegible]	M.L.D. [illegible]	[illegible]	M.L.D. [illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]			[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]			[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

M.L.D. [illegible]
†The footnote of Lapschitz on [illegible] M.L.D. was checked and confirmed by the author of this paper
‡Not tested

quinoline ring of quinine and the diethylaminoethanol radical found in many of the procaine series (a-butyloxycinchonic acid diethylaminoethylene diamide hydrochloride) It was synthesized by Karl Miescher and studied by Uhlmann Lipschitz and Laubender (35) and others Though it has been often described it is so little understood that its abuse rarely its legitimate use has resulted in frequent deaths To this point we shall return later The fact that in spite of these accidents its use is apparently increasing proves the urgent need for local anesthetics with a prolonged action

Drothane has a substituted phenyl urethane radicals contained in a total molecule which is otherwise suggestive of the procaine series It has been synthesized by Rider and suggested for prolonged local anesthesia (50, 51)

Benacol is a solution of equal parts of paramino benzoyl benzoate and phenmethylol in 90 parts of rectified sweet almond oil It has been used extensively by Yeomans and his associates in the treatment of intractable pruritis and In England It is used at St Mark s Hospital by Gabriel for pruritis and and anal fissure H T Hayes, in Houston, has used it also at the close of hemorrhoidectomies injecting small amounts under the operative wound to give prolonged local anesthesia.

Anocaine is a new preparation in oil resembling benacol but having in addition one part of butylamino benzoate and ½ part of novocain base

Procaine hydrochloride concentrated in a solution of 5 per cent has been mentioned by Schmidt as giving a longer anesthesia than nupercaine 1 1000 when both are used with adrenalin As such a strong solution of procaine is less toxic than the weak solution of nupercaine it was included in the determination which follows.[1]

Tutocaine hydrochloride is a member of the procaine series which is about twice as potent as procaine hydrochloride and only half as toxic on subcutaneous administration to animals Instead of the ordinary ¼ to ½ per cent solution it was tried for prolonged anesthesia in a concentrated solution of 2½ per cent

Before comparing the local irritation caused by these solutions, it is well to have in mind their general toxicity

COMPARATIVE TOXICITY

The comparative toxicity of these solutions must be considered from the standpoint of exact measurements in animals and then also from clinical experience

Animal experimentation Measurements of toxicity in animals are shown in Table I In this table there is included for comparison the well known anesthetics of short duration, procaine and tutocaine The first column lists the solutions in concentrations effective for anesthesia. The second column shows the amount of clinically effective solutions which would be lethal subcutaneously to a 70 kilogram man if he were equally sensitive to the solutions as the rabbit In the fourth column is shown the minimal lethal dose intravenously in the rabbit In the fifth column is

[illegible]

TABLE II —PROTECTION BY NEUTRALITY (ACID BASE), ISOTONICITY, AND URETHANE AGAINST LOCAL IRRITATION BY QUININE SALTS—0 15 CUBIC CENTIMETER INTRADERMAL WHEALS IN RABBITS' FLANKS

		Results	Per cent sloughs
1 a	Quinine HCl 1/5% in quinine urea diHCl 1/5% in water	oeoeoooooeo	
1 b	Quinine HCl 1/2% in quinine urea diHCl 0 7% in water	oSoooooooo	
2 a	Quinine HCl 0 7% in quinine urea diHCl 1% in water	SoeoooeoSo	
2 b	Quinine HCl 0 7% in quinine urea diHCl 1% in .425% saline	oooooooo	
3	Quinine HCl 1% in .425% saline	SSSSSSoS	88
4	Quinine HCl 1% with urea 0 17% in quinine urea diHCl 1.4%	eSSSeSoSoo ooSSeSoSSoSoSoSo	46
5	Quinine HCl 1% with urea 0 5% nearly neutral in .425% to 0.85% saline	Sooeoeeo SoeoSeoooe	17
6	Quinine HCl 1% with urethane 0 5% fresh mixture (nearly neutral) in .425% to 0 85% saline	oSeoooooooo oooSoooe	12
7	Quinine HCl 1% with urethane 0 25% fresh mixture—adrenalin 1 1000 5 c.cm in 0.85% saline 100 c.cm	SeeSoeo	
8	Quinine HCl 1% with urethane 0 5% old mixture (nearly neutral) in 0 85% saline	oooooooooooeee	0
9	Quinine HCl 1% with urethane 0 5% old mixture (nearly neutral) in 0.85% saline with adrenalin	oeoeeeeeoo oooooo	0

*S Sloughs e Erythema o No sloughs

shown the amount of clinically effective solution given intravenously which would be lethal to a 70 kilogram man if he were equally sensitive to the solution as the rabbit

No previous record of the minimal lethal dose of eucupin administered sucutaneously to the rabbit has been located in the literature Accordingly, 0 150 per kilogram body weight of eucupin base or 0 170 per kilogram body weight of eucupin dihydrochloride was injected subcutaneously into 8 rabbits and they were kept alive for 14 days None of these died or showed the slightest toxic symptoms Two rabbits were given 0 300 kilogram per body weight of eucupin base subcutaneously One lived and one died within half an hour The minimal lethal dose to the rabbit must, therefore, be over 0 150 per kilogram body weight subcutaneously Bijlsma gave 0 025 per kilogram body weight subcutaneously to one kitten and the kitten died on the sixth day I have given 4 times this dose to 2 kittens without the slightest toxic symptoms for 6 days

It will be seen from Table I that when solutions of equal anesthetic potency are injected into the rabbit, eucupin solutions may be used safely in the largest amounts and nupercaine in the smallest amounts In these concentrations more than twice as much eucupin solution may be injected into the rabbit subcutaneously as procaine hydrochloride and thirty times as much solution of eucupin base as nupercaine solution of equal anesthetic power Indeed if man were equally susceptible to eucupin as is the rabbit, and water intoxication be disregarded, the amount of clinically effective anesthetic solution required to be lethal by subcutaneous infiltration would be about 3 gallons[1]

Although the toxicity of solutions administered subcutaneously varies in different animals including man the intravenous lethal dose per kilogram body weight does not have such wide variations, and, therefore, the comparison of intravenous toxicity is shown (Table III) Here again the superiority of eucupin in freedom from toxicity is shown as well as the limitations of nupercaine

Clinical estimate From the clinical standpoint, we find that quinine hydrochloride urethane in a highly concentrated solution has been injected into man intravenously in varicose veins several hundred thousand times with only one reported fatality from toxicity (Matas)

The possibility of peculiar individual susceptibility to eucupin has been investigated by Dawson and Garside, who found that because of the long and branched side chain in

its molecule, natural idiosyncrasy to eucupin is unlikely (8) although idiosyncrasy may be acquired (7)

Twenty four deaths from nupercaine have been reported (see appendix) When it is used we should be on our guard against its toxicity using these precautions First large doses of barbiturates should be given before operation as this probably gives protection against its toxicity (63 64 69) Second in view of the considerable number of deaths known to be due to injection of solutions made by mistake 10 times too strong in 1 per cent instead of 1/10 per cent it is safer not to resort to the local pharmacist to make up the solution but to use the large 25 cubic centimeter ampules of 1 1000 solution recently made available by the manufacturers. Third in view of its extraordinary toxicity if injected into a vein or venous sinus, the technique of local infiltration must be perfect in order to prevent such an eventuality especially when in hemorrhoidectomy injection is made near a ligated blood vessel. *Fourth, in view of a fatality* with only 90 cubic centimeters 1 1000 solution injection of concentrations greater than 1 1000 or in amounts greater than 50 cubic centimeters should be made with caution

LOCAL IRRITATION

There is a need for a new method for measuring tissue irritation caused by local anesthetics which I shall submit Older methods have had partial values

Anesthetic solutions for a long time have been injected into rabbits ear lobes where the skin on the outer side of the lobe comes close to the skin on the inner side of the lobe, to see if they would cause sloughing. Experience in this method (32) has shown that it is not sufficiently delicate for a test of local anesthetics For example it has been found that small amounts of 2½ per cent quinine urea dihydrochloride do not make sloughs by this test and even 5 per cent of the same solution does not always do so but there is abundant clinical evidence to show that a 2½ per cent solution of quinine and urea dihydrochloride may cause sloughing

Another test instills the anesthetic solution into the conjunctival sac of the rabbit to see if conjunctivitis follows. This method lacks a sharp endpoint. It measures the effect on topical application to a peculiarly developed structure rather than the effect of infiltration. It allows only 2 tests on each animal, whereas the test which is to be submitted allows 8 or more tests to be made on each animal and measures the direct effect of infiltration.

A third test measures the hemolytic action of the solution to be tested on red blood corpuscles. This test, while not new has recently been explored thoroughly by Schmidt and has considerable value. However it has certain handicaps It assumes that a non nucleated red blood corpuscle will respond to possible irritation by local anesthetics, as do the nucleated cells of the tissue. Imagine here the bizarre results which must be expected if a hemolysis test were made on such a solution as quinine urethane, inasmuch as we know that urethane acts to take quinine promptly out of serum to fix it in the red blood corpuscles (40) It does not take into account the vasoconstrictor or vasodilator effect of the solution to be tested, on the local circulation. It does not allow measurement of the effect on irritation, of such added substances as adrenalin and urethane, which we shall show to be important. In practice, it does not check with infiltration tests For example Bijlsma found that vuzin dihydrochloride had only half the hemolytic effect of eucupin dihydrochloride on erythrocytes suspended in Ringer's solution, and that even when serum was added the effect was about equal (3) Yet the experiments which I shall report indicate that vuzin dihydrochloride when infiltrated is more irritating than eucupin dihydrochloride This may be explained by the fact that eucupin is a vasodilator and vuzin a vasoconstrictor[1] (Bijlsma) Hemolysis tests do not take into account such action

The method to be submitted uses intradermal wheals made in the flanks of rabbits If this method has not been used before it is probably because of the difficulty in removing the hair Shaving the rabbit's hair plucking it, or using a depilatory must be avoided, since all such procedures cause so much irritation as to interfere with measurements of

[1] [illegible]

the irritation due to the solution injected A high speed electrical veterinarian's clippers, on the stretched skin, if aided by frequent brushing of the hair from its teeth, will remove the hair close to the skin without irritating it Two or three such patches are made in each flank, between the ventral and dorsal areas Care must be taken to keep away from the gluteus maximus and biceps femoris muscles, as sloughing is more likely to occur in this region If the patches are too close to the artery located over the shoulder, sloughs which would occur elsewhere would not be observed If the hair which remains interferes with the observations, it should be wetted Two injections of 0 15 cubic centimeter each are made into each one of the two patches, making 8 in all In case uniform results are not obtained, a much larger number of injections may be made

These intradermal injections make a delicate test because the solution lies under the horny epidermal cells with poor blood supply and, therefore, a slough is more apt to occur by this method than in ordinary tissue infiltration Comparison with the wheals that have been produced in the skin of the human thigh indicates that rabbit skin is more sensitive The delicacy of this test can be still further increased by the addition of adrenalin to the solution

In the protocol which follows, it will be noted just what concentrations of nupercaine, eucupin solutions, quinine urea dihydrochloride, quinine hydrochloride and urethane, diothane, and benacol and anucaine can be injected in amounts of 0 15 cubic centimeter intradermally in the rabbit with and without sloughing These tests have been made with aqueous and isotonic solutions, with and without adrenalin An "S" is marked where a slough occurred, an "o" where there was no change, and an "e" where there was erythema without sloughing I made more than 1,300 of these wheals in rabbits and give reports where the findings proved of practical significance

The optimum solution for quinine It will be seen from Table II that the highest concentration of quinine and urea dihydrochloride in water which can be used without sloughing is ½ per cent quinine and urea (containing ⅓ per cent quinine hydrochloride) This is important because it shows that this laboratory method agrees in results with clinical experience in the thousands of cases reported by Crookall, Finsterer, and Saphir

Quinine hydrochloride in 1 per cent solution in saline gave sloughs in nearly every wheal (88 per cent sloughs) When the same concentration of quinine hydrochloride 1 per cent was used in ordinary quinine urea dihydrochloride 1.4 per cent, less than half (46 per cent sloughs) of the wheals sloughed This shows that the addition of urea does prevent some of the irritation of quinine, as is generally accepted But a very much greater improvement came when (a) the amount of urea was increased to 0 5 per cent, (b) no hydrochloric acid was added, and (c) 0 425 per cent saline was used instead of water (17 per cent sloughs)

Still greater was the improvement when urethane was substituted for urea A fresh solution of quinine urethane caused only 12 per cent sloughs A well aged solution of quinine hydrochloride and urethane kept for 3 weeks showed no sloughs at all Even when adrenalin was added (and we shall see later that the addition of adrenalin increases greatly the tendency of most solutions to slough), a well aged solution of quinine urethane was used in 18 wheals without a slough One may conclude that about three times as strong a concentration of quinine hydrochloride can be used in a well aged solution with 0 5 per cent urethane, even with adrenalin added, without sloughing, as can be used when made up with urea and hydrochloric acid in water in the ordinary quinine and urea dihydrochloride This is the first advantage of quinine urethane solution over quinine and urea dihydrochloride

A second advantage is that quinine urethane keeps better than weak solutions of quinine and urea dihydrochloride, which tend to deteriorate because, as Giemsa found (16), the urea decomposes to form alkaline ammonium which precipitates the alkaloid quinine, and this process probably is accelerated when the quinine and urea are in a less acid solution This may be the reason, certainly

a good one why quinine and urea have been used in an acid solution But when urethane is added this trouble is avoided for it has been known for a long time (16)—and I have confirmed this—that quinine with urethane if not saturated does not precipitate on standing

There is a third reason for the superiority of quinine hydrochloride with urethane over quinine urea dihydrochloride quinine and urea dihydrochloride causes an immediate violent pain at the site of injection. Quinine urethane causes little if any such pain as any one may verify

Fourth intracutaneous wheals were made by injecting urea dihydrochloride and quinine hydrochloride urethane The first showed a wide border of erythema around them the quinine hydrochloride urethane did not This indicates that quinine urethane is less irritating

One may conclude that a well aged solution of quinine hydrochloride urethane with sodium chloride added to isotonicity and adrenalin, is superior to the classic solution of quinine and urea dihydrochloride

Protective action of urethane It has been known to Frohlich to Winkler and to Dansen Peng that the systemic administration of urethane in large doses inhibited the irritant action of mustard oil on the skin, but no previous reference has been found to the fact that infiltrated locally small concentrations of urethane added to quinine have a protective action against irritation and sloughing

The change which urethane makes is not that it merely prevents inflammation Inhibition of inflammation might actually lessen the resistance of the tissue to injury But my experiments show that it actually prevents tissue injury and sloughing

The action does not seem to be on the pain nerves for while urethane 5 per cent is anesthetic, concentrations below 2½ per cent are not (23) It does not seem to protect by action bringing in a better supply of blood and serum to the site of injection because there is less redness around a wheal into which quinine urethane is injected than when wheals are made with quinine urea dihydrochloride or nupercaine That urethane like urea has a lytic action on the fibrin (42) laid down by quinine and thus prevents irritation is one possibility Another is that the protective action of urethane is exerted not on the tissues but chemically on the quinine It has been noted that when urethane is added to quinine there is a change in the lines of the absorption spectrum (19) This has been ascribed by de Thron (10) to the formation of quinicin or quinotoxin an isomere of quinine which Sollmann (61) showed was, contrary to its name not exceedingly toxic However the quinotoxin occurs only in 3 per cent in de Thron's findings, and one therefore questions whether this can explain the protection conferred by urethane against tissue injury It might seem more probable that the urethane combines with the quinine[1] probably at the unsaturated double bond in the vinyl side chain In this connection it may be noticed that nupercaine, the least irritating of the quinolin anesthetics also has a structure suggestive of a substituted urethane

The fact that aging of the solution of quinine urethane makes it less irritating may be explained on two grounds Either time and sunlight allow the urethane to become more thoroughly united with the quinine molecule or else the quinine turns to quinicine (quinotoxin) This problem is now being studied

Effect of osmotic pressure It will be seen from a study of the controls in Table IV that 3 wheals made with distilled water out of 18 caused small sloughs whereas none of the 12 made with physiological saline made sloughs. This shows the importance of isotonicity even without the addition of adrenalin

A further study of the controls shows that procaine hydrochloride and tutocaine hydrochloride can be used in aqueous solutions with adrenalin, without sloughing This, however does not hold at all for the other solutions

In the case of nupercaine although the manufacturers rightly advise its use in saline the importance of this is not generally realized. I have found one of our ablest surgeons using

[1] Marks has shown on the long chain in contrast to many other anesthetics, urethane and ethylhydrocuprine cause only slight inhibition of leucocytic migration

[1] Marks has shown that urethane exerts prolonged changes on the physiological action of epinephrine depressing it out of the blood vessels and leaving in the blood circulation for 48 hours and at the same time hastening its elimination from the kidneys

TABLE III —TISSUE IRRITATION BY LOCAL ANESTHETICS, 0 15 CUBIC CENTIMETER INTRACUTANEOUSLY IN RABBITS' FLANKS

Solution	In water	Approximately isotonic	In water with adrenalin	Approximately isotonic with adrenalin†
Distilled water or saline	ooooSoSSoo	oooooooooo	oSoeoooo	oooooooo
Procaine HCl 1%			oooooooo oooooooo	
Tutocaine HCl 1%			oooooooo	
Procaine HCl 5%			oooooooo	
Nupercaine 4/10%		ooooSeeee		
Nupercaine 3/10%		oooooooo		oooooooSS
Nupercaine 2/10%			eSSoSSSS	oooooooo
Nupercaine 1/10%	oooooooo		SeeeeSSS	oooooooo
Eucupin base 1/10% HCl 10% 2 c.cm. in 100 c.cm Tutocaine ½%	ooeSSSSoooooo	oooooooeeooo	oSooSSSSo	oooSeSSoooooooo
Same with urethane ½%				oooooeoooSo SeSeooeS
Eucupin base 1/10% HCl and NaOH to dissolve procaine HCl 1%	SoooSoSo	oooooooooo‡		
Vuzin base 1/10% in Vuzin diHCl 11/100% 10% HCl 5 c.cm to 100 c.cm				SSoeoSeoSS
Eucupinotoxin in 2/10%				SSooSSSe
Diothane 1%	SSSSSSSSSo	oeeSSSoo		
Diothane ½%		oSoooooooooooooee oooooooooooSSoo SSooSSeeoo		
Diothane ⅓%	ooSeSoSo			
Benacol (oily)	SSSSSSSS			
Anucaine	SSeSSSSS			
Nupercaine in oil	oSSSSSSSSSSSSSS SSSSSS			

S Sloughs e, Erythema o No sloughs*

*In some early experiments where erythema occurred without sloughing a zero was recorded

†Adrenalin was used 0 5 c.cm of 1 1000 solution in 100 c.cm

‡No procaine hydrochloride added

nupercaine in an aqueous solution The experiments in Table III show that nupercaine 1 1000 in water with adrenalin is likely to cause sloughing Twice as great a concentration can be used with adrenalin in saline without sloughing

Again, in the case of eucupin, tests show (Table III) the importance of isotonic rather than aqueous solutions, illuminating one of the mysteries of medical history De Takats of Northwestern University, performed over a hundred operations with eucupin in saline without a single slough One hundred intradermal wheals which he made caused no sloughs Then other workers (44) used it in solutions which were "water solutions in the majority of cases" and had sloughs As a result of their condemnation, the surgical world did nothing further with eucupin How did it happen? The protocols in Table III show that both sides were right in their experiments Twenty-one wheals made with eucupin hydrochloride in saline caused no sloughs Twenty wheals made with eucupin hydrochloride in distilled water did show frequent sloughs [1]

Clinicians sometimes assume that because sodium chloride 0 85 per cent is isotonic with

[1] I must warn against the solution tried by Picard which is made in water in 0 2 per cent and is likely to cause sloughing

Fig. 1. Sites for intracutaneous wheals for tests of local irritation by anesthetic solutions.

body fluids, procaine hydrochloride is isotonic in the same concentrations. This is a wrong assumption. Procaine hydrochloride is not *isotonic in 1 per cent but in 5.48 per cent* (4). Eucupin in a 1 per cent procaine solution or a half per cent tutocaine solution is far from being isotonic.

Effect of adrenalin. The results of experiments with the addition of adrenalin shown in Table III were an unpleasant surprise. The addition of adrenalin is necessary for the prolongation of analgesia for several days. Yet *these experiments show that in all these solutions tested except procaine and tutocaine* the addition of adrenalin greatly increased the tendency to tissue injury. This was unfortunately true to a marked degree with eucupin.

Effect of acidity on eucupin. Table IV shows the desirability of keeping anesthetic solutions, such as eucupin, away from the acid side. This agrees *exactly with tests* on the conjunctival sac made by Sollmann (60), by Copeland (5) and by Gifford (18), showing less irritation if solutions are kept nearly neutral. However, a solution buffered in borax boric acid, made on the suggestion of Gifford's work, was not free from sloughing tendency when adrenalin was added.

Vanay is shown by the tests to be more irritating than eucupin.

Diothane. I have no judgment to pass on diothane for topical application, but the tests made for infiltration in Table III show that in aqueous solution, the form in which it is recommended, it has a pronounced sloughing tendency. The addition of saline partly helped this but caused an early precipitation of the diothane.

TABLE IV.—EXPERIMENTS TO MODIFY TISSUE IRRITATION BY EUCUPIN

0.15 CUBIC CENTIMETER INTRACUTANEOUSLY IN RABBITS' FLANKS

All solutions approximately isotonic

Effect of pH.	Without adrenalin	Adrenalin [illegible] per cent solution
[illegible]	[illegible]	
[illegible]	[illegible]	
[illegible]		[illegible]
[illegible]		[illegible]

*Hydrogen ion concentration taken from report of Copeland and Nelson.

[illegible] Slough. [illegible] Erythema. [illegible] No slough.

Benacol had a destructive action. Sloughs were large and deep. It would seem to be painful, for even the long suffering rabbit who did not squirm upon the injection of any other solution except distilled water jumped and squirmed, or actually cried out in loud squeals when wheals were made with benacol. It may be desirable for the destruction of subcutaneous nerves in pruritis ani, but one feels reluctant to class it as a local anesthetic.

Anucaine was equally destructive, causing sloughs in nearly every wheal. So also did nupercaine in oil.

Although an anesthetic solution for the purposes of rectal surgery to be described must not cause too much irritation, it is not necessary that such a solution have the perfect freedom from irritation *which is a sine qua non* of general surgery.

First, in general surgery there must be prompt union of the tissue layers and such union must not be delayed. In rectal surgery many of us prefer to leave wounds wide open to be healed by second intention. Second, it is known that solutions which might cause sloughing if injected in an area where the tissues are under pressure will not cause sloughing if there be no pressure or tension. In closed surgery with the wound sewed up

tight, there is postoperative tissue edema and sometimes pressure This is avoided in open types of rectal surgery Third, in rectal surgery a cause of delayed healing is the spasm of the sphincter muscle after operation, which grips the operative wound so tight as to cause ischemia Prolonged local anesthesia prevents this vise-like grip of the sphincter, prevents the ischemia and thus facilitates healing Fourth, in rectal surgery in the lower area in the skin below the mucocutaneous line, delayed healing may be actually desired when fissures and infected crypts need prolonged surgical drainage

On the other hand one has reason to protest against the common use, even in rectal surgery, of some of these irritant, if not destructive, solutions There is especial danger of postoperative hemorrhage when such solutions are injected into the anal canal near the large branches of the inferior hemorrhoidal artery

COMPARATIVE ANESTHETIC POWERS

Of the large number of methods previously devised to measure the anesthetic power of solutions, two are of outstanding importance First, the intracutaneous wheal to measure the potency of anesthetics for infiltration, and second, instillation into the rabbit's conjunctival sac to determine whether or not the solution paralyzes the corneal reflex It will be shown later that deduction from the rabbit's cornea test, if applied to oily solutions, may lead to errors, and a new test will be presented to measure the power of local anesthetics on topical application, utilizing directly the open wound

In using tests on the intracutaneous wheal, I have sought to avoid errors made in the past How unsatisfactory past methods have been is shown by the wide divergence in results For example, in measuring the duration of anesthesia in the wheal made by procaine hydrochloride, pharmacologists of high standing report results in the wheal made by procaine hydrochloride varying from 9 minutes to 35 minutes, and in the wheal made by nupercaine, a duration varying from 35 to 100 minutes (28) Exactly the same amount of anesthetic must be injected into the wheal or

Fig 3 Testing of surface anesthesia with Harvard inductorium

wide variations in the duration of anesthesia will result I have used 0 4 cubic centimeter because this gives a large enough wheal to avoid doubtful readings Still more important is the choice of an instrument to test anesthesia in the wheal The wisp of cotton the pin prick, and the blunt wire all cause error, because the tip may contact a point in the skin between nerve endings An associate tested the skin of my forearm with the twisted wisp of cotton and found that in 3 places of 15 so tested without any previous injections of anesthetics the wisp of cotton could not be felt A stroke with a pin, or the use of an electric current between two terminal wires covers enough space to catch a nerve ending, which may be missed by contact at a point The pin scratch method has the advantage of avoiding the irritation caused by the electric current On the other hand, the electric current has the advantages of giving a clearer endpoint and of measuring pain sensation without admixture of touch and pressure sensation In these experiments electrical stimulation was used between the ends of 2 fine wires conveyed from an inductorium

The first column in Table V shows the duration of anesthesia when adrenalin was not added to the solutions The solution of quinine urethane gave a much longer anesthesia than the solution of quinine urea dihydrochloride Nupercaine gave anesthesia of shorter duration than eucupin

The second column shows that when adrenalin was added, nupercaine gave a more prolonged anesthesia than eucupin with tutocaine and adrenalin [1] Nupercaine with tutocaine

[1] De Takats in wheals on the forearm, obtained anesthesia for 7 hours from the eucupin tutocaine adrenalin solution My results show a much shorter duration but my tests with electrical stimulation give a much stronger stimulation than the skin scratch which he used

gave a still longer anesthesia. Quinine hydrochloride with urethane gave a partial anesthesia lasting for more than 3 days

Procaine hydrochloride with adrenalin concentrated in 5 per cent gave longer anesthesia than nupercaine 1 1000 with adrenalin. A strong solution of 2½ per cent tutocaine gave a still longer anesthesia.

It should be emphasized that these wheal tests are only of value in giving an idea of the duration of anesthesia by one solution as compared with another They do not give an idea of the absolute duration of analgesia. Although eucupin tutocaine adrenalin solution gives *anesthesia for not over 2 hours by* my tests in the wheals, clinical experience agrees with that reported by de Takats,[1] that this combination sometimes gives analgesia for about 3 days

PROLONGED ANESTHESIA BY TOPICAL APPLICATION

Attempts to produce prolonged anesthesia by topical application to the open wound date back to 1911 when Vogel of the University Clinic of Marburg, applied a 2 per cent solution of eucupin with adrenalin to the pharynx after tonsillectomy Such attempts failed for several reasons First, the addition of adrenalin to eucupin solutions invalidates them for topical application when adrenalin is added to eucupin for *infiltration* the anesthetic action is prolonged because the vasoconstrictor action of the adrenalin prevents the removal of the anesthetic away into the general circulation and causes it to exert its action locally in full force. When adrenalin is added for topical application the opposite effect is obtained the vasoconstriction resulting from the adrenalin prevents local absorption of the anesthetic solution, so that little if any of the anesthetic gets into action.[2] Previous solutions of eucupin for topical application (74) have been used in very high concentrations which were too irritating Finally in earlier days but little was known as to preventing the stinging effect of strong solutions of eucupin when applied to the open wound.

It is commonly assumed that the rabbit's cornea test may be used to estimate the comparative potency of anesthetics for topical application to other surfaces such as the open wound. That this common assumption may lead to egregious errors seems indicated by experiments hereinafter described. It is true that the rabbit's cornea test gives some idea of the comparative potency of aqueous solutions but it is quite unreliable as a measure of the potency of solutions in oily bases on the open wound Morgenroth long ago showed *that oily solutions of the bases of eucupin* and other hydrocupreines anesthetized the rabbit's cornea. I have tried the same experiment with nupercaine ointment on the rabbit's *cornea and obtained excellent anesthesia.* Probably because of such findings, we are now having it advertised for local application for prolonged anesthetic effect to all sorts of open wounds and mucous membranes but especially to rectal wounds.

Clinically nupercaine ointment applied in the open wound does not begin to give any such anesthesia as ought to be expected from its powerful anesthetic action on the rabbit's cornea. Accordingly a method was devised for measuring the potency of local anesthetics topically applied to the open wound. In *rabbits, under ether anesthesia, the peri-anal* skin and mucous membrane were removed down to and partly into the sphincter muscles. After the animal had entirely recovered from the anesthetic, an electric current was applied to the wound from an inductorium strong enough to make him jump. On one side nupercaine or other ointments were then applied on the other side eucupin solutions were applied. These were held in contact for 5 to 8 minutes. Then electrical stimulation was applied to each side and the results compared. It is necessary not to hold the tail up, as this inhibits reaction.

When this test with nupercaine ointment was made on 13 rabbits, not once was anesthesia obtained. Every time, stimulation made the *rabbit jump* where nupercaine ointment had been applied On the other side in all of 7 rabbits tested eucupin solution from ½

[1] De Takats, in wheals on the forearm, obtained anesthesia for 2 hours from the thermal [illegible] adrenalin solution. My results show much shorter duration, but my tests with electrical stimulation give much stronger stimulation than the skin scratch which he used.

[2] Agreeing with the work of Sollmann who found that the addition of adrenalin interfered with the action of quinine urea hydrochloride on the rabbit's cornea (94)

per cent to 9/10 per cent in water always produced partial anesthesia and usually complete anesthesia Eucupin ½ per cent in physiological saline solution was not so effective as the eucupin in water [1]

Nupercaine 1 per cent solution was not tested against the 1 per cent nupercaine base in ointment because strong solutions of nupercaine are too toxic to be used in large amounts

Someone may inquire, "But does not an oily solution act better because it stays there longer slowly feeding out the anesthetic?"

This might be true of an anesthetic of short action, but we are now dealing with anesthetics which after absorption in the tissues give a prolonged action As a matter of fact these anesthetics are so extremely soluble in oily bases as compared with the tissues that they are not absorbed well from their nest in the oily base Possibly the reason why they do anesthetize the cornea and not the open rectal wound may be found in the fact that the cornea has neither blood vessels nor lymphatics which would carry away the absorbed drug Moreover, the nerve fibers in the cornea are non-medullated

TABLE V —COMPARATIVE DURATION OF ANESTHESIA — INTRACUTANEOUS WHEALS, 0 4 CUBIC CENTIMETER ON ABDOMEN — 3 WHEALS WITH ADRENALIN — 4 WHEALS WITHOUT ADRENALIN—TEST WITH HARVARD INDUCTORIUM

Solutions	Without adrenalin	With adrenalin*
1 Physiological saline (control)	No anesthesia	
2 Distilled water	Less than 35 min.	
3 Quinine urea dihydrochloride in water 0 5%	1 hour 20 min	
4 Quinine urea dihydrochloride 0 5% in saline	Less than 45 min	
5 Quinine hydrochloride 1%	Complete 1 hr 30 min	Complete 5 hours
Urethane 1/5% in physiological saline	Partial 5 hours	Partial 3 days
6 Nupercaine 1/10% in saline	1 hour	Between 2 and 3 hours
7 Nupercaine 1/10% in saline with tutocaine 0 5%		3 hours 15 min
8 Eucupin base 0 1%	Complete 1 hr 30 min	Between 1½ and 2 hours†
Hydrochloric acid 0 2% Tutocaine 0 5% in saline	Partial 2 hours	Partial 3 hours
9 Procaine HC 5% in water		3 hours 10 min
10 Tutocaine HC 2½% in 0.425 saline		4 hours 10 min
11 Eucupin base 1% in rectified sweet almond oil (one wheal only)	No anesthesia—redness and pain	

*Adrenalin 1 1000 was added 0 5 c.cm to each 100 c.cm of solution
†When adrenalin 0 1 c.cm was added instead of 0 5 c cm the duration of anesthesia was unchanged

CLINICAL FINDINGS

From the laboratory findings presented, one should expect quinine urethane solution to be far superior to all other known local anesthetics of prolonged action, because, when such solutions, in the highest concentrations which can be used without sloughing are compared, quinine urethane solution gives by far the longest anesthesia Clinical experience, however, raised an unexpected difficulty when quinine urethane solution was used for infiltration in operative surgery it prolongs the bleeding time so that the wound may ooze for 2 or 3 days For this reason it was abandoned in operative surgery

On the other hand quinine urethane has justified expectations for the purpose of injection of anal fissure It can be used in a higher concentration without sloughing than can quinine urea dihydrochloride, it is more stable, and, most important, it does not cause such severe pain on injection as quinine urea dihydrochloride Of course any anesthetic solution, even procaine hydrochloride, will cause pain if injected under some hypersensitive fissures, but quinine urethane solution is much less likely to cause pain than quinine urea dihydrochloride It is now being used in a concentration of quinine hydrochloride 1 to 3 per cent, with urethane in half the concentration of the quinine Usually 1 or 2 cubic centimeters are injected under a fissure

Quinine urethane solution may also prove of value in the injection treatment of pruritis ani [2]

It must be warned that the supersaturated solution of quinine urethane used for varicose

[1] Similarly Hertzler found that in aqueous solution the absorption of procaine hydrochloride by the peritoneum was more rapid than when the procaine was dissolved in physiological saline

[2] If quinine urethane is mixed with novocain suprarenin solution "K," which is the common form sold in ampuls a gelatinous precipitate forms This is due to potassium sulphate added to the ampul as a stabilizing agent which precipitates quinine. This difficulty can be avoided by using ordinary bulk procaine hydrochloride or a tablet of tutocaine

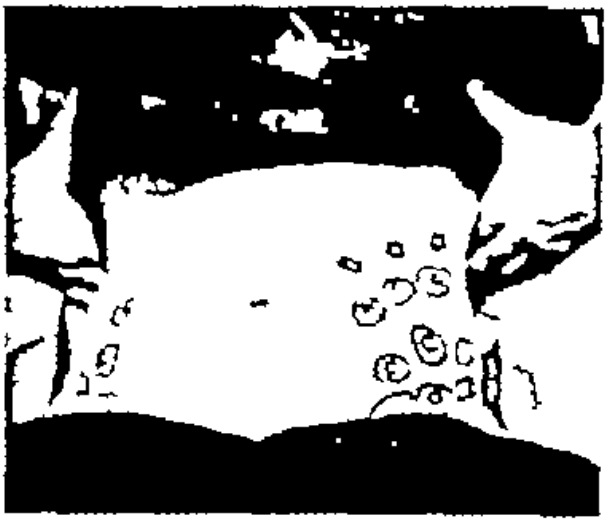

Fig 4 Bites of wheals to determine duration of anesthesia Note absence of areola of redness around quinine urethane wheals

vein injection is too strong for any of these purposes.

EUCUPIN FOR TOPICAL APPLICATION

Three-fourths per cent eucupin base with just enough 10 per cent hydrochloric acid added drop by drop to dissolve, in water has proved to be of great value in postoperative wounds after fistulectomy excision of pilonidal sinuses, and hemorrhoidectomy Indeed in large fistulectomy wounds infiltration is impracticable and topical application is the only method available. Eucupin solution, not nupercaine solution should be used for this purpose because nupercaine solution is too toxic to be used in the high concentrations and large amounts needed for topical applications. Eucupin is also relatively inexpensive The same patient who has had nupercaine ointment applied with little or no relief will tell you that there is no comparison between the two methods that after the eucupin solution there is complete relief of pain sometimes for 12 hours or more

Eucupin 0 75 per cent solution is also being applied topically in cases of prolapsed strangulated gangrenous hemorrhoids. Such cases are not usually operated on by competent proctologists in this stage Eucupin applied both relieves pain and keeps down infections

One of the chemists who prepared the 0 1 per cent solution of eucupin buffered in borax boric acid, heretofore described, dropped this into his nose for the relief of hay fever Ephedrine gave him relief for only 15 minutes This eucupin solution made his nasal passages perfectly clear for 24 hours and nearly clear for a second 24 hours.

TECHNIQUE OF EUCUPIN APPLICATION

Upon topical application of eucupin 0 75 per cent solution in the open wound, there is sometimes a stinging which may last 5 to 15 minutes. For this reason, it should be applied before the anesthesia obtained prior to operation has worn off. Its anesthetic action will then last so long that reapplication of eucupin can be made before anesthesia from the first application has worn off Cotton does not stick to the wound as does gauze at the time of reapplying fresh eucupin. The cotton soaked with eucupin should be pressed into the wound for 5 full minutes and then left in the wound. It may then be reapplied in the same way every 3 hours for four times. Then the eucupin soaked cotton should be taken out and left out More prolonged use is unnecessary and may delay healing of the wound

HEMORRHOIDECTOMY WITH PROLONGED LOCAL ANESTHESIA

It is not to be expected that pain after hemorrhoidectomy can be avoided when the ligature or the various closed suture operations are performed In order to make the patient comfortable the open Pennington operation has here been followed, which dissects out the whole external and internal hemorrhoid down to the sphincter fibers and out in triangles of skin and then picks up the hemorrhoidal vessels in as small a bite of the hemostat as is possible for double transfixion and ligation The new operating speculum devised by Fansler makes comparatively easy this, which is otherwise a difficult, operation

Spinal or sacral anesthesia is rarely and general anesthesia never used Anesthesia has been obtained by blocking of the branches of the internal pudendal nerves in the ischiorectal fossa Tutocaine has been used for this purpose because it is twice as potent and about half as toxic as procaine hydrochloride

In the earlier cases, eucupin 0 1 per cent in physiological saline with adrenalin was in-

filtrated at the close of operation under the wounds Later nupercaine 0 1 per cent solution in physiological saline with adrenalin, for infiltration was used, fortified by the topical application of eucupin 0 75 per cent solution by the technique heretofore described.

Now, all infiltration by these solutions has been abandoned and eucupin 0 75 per cent in water by topical application to the open wounds by the technique described is used alone This is usually sufficient The eucupin thus topically applied has a great added advantage in its powerful bactericidal action which causes it to prevent infection in this field exposed to contamination

Clinical results Stress had been laid on controlled laboratory measurements, because clinical findings can prove the comparative value of these local anesthetics only when very large numbers of cases with very large numbers of controls are available This is especially true in this rectal problem where patients vary so greatly in their susceptibility to pain Clinical results given are presented, not as demonstrations, but as suggestive After 100 rectal operations, patients were told that they could have as much narcotic as they pleased—usually morphine or codeine Of these, 14 wanted one dose of narcotic, 13 wanted more than one dose, while 73 did not want any narcotic at all This makes 87 per cent who were free or nearly free from serious pain for the 3 days after rectal surgery! Of these a few had barbiturates the night after operation to prevent restlessness and most had barbiturates before operation Three radical operations for internal and external hemorrhoids were performed in the office under local anesthesia To each of these patients a prescription for codeine was given Two of the three never had the prescriptions filled as they had no need for the codeine Another patient, seen in the hospital 7 hours after a radical hemorrhoidectomy, complained strenuously because he was kept in the hospital saying "I feel perfectly well I want to get up and walk home!"

SUMMARY

1 An improved method for measuring local irritation by local anesthetics was used in 1 300 tests The highest concentrations which can be used without sloughing were determined for nupercaine, eucupin, quinine urethane Similar tests were made of tutocaine hydrochloride procaine hydrochloride benacol anucaine, nupercaine in oil, diothane, and quinine urea dihydrochloride Vuzin proved more irritating than eucupin

2 Topically applied in the open wound by a technique described, eucupin 0 75 per cent solution gave excellent results after operations for anal fistula pilonidal sinus and hemorrhoids It may also be applied to prolapsed strangulated gangrenous hemorrhoids Its bactericidal qualities in addition to its prolonged anesthetic action enhances its value in rectal wounds subjected to contamination

3 After 100 rectal operations in which prolonged local anesthetics were used, narcotics were offered freely to all but 73 per cent of the patients were so free from pain that they wanted no narcotic

4 A solution of quinine urethane not in the concentration used in varicose veins proved the best of these solutions for injection treatment under anal fissure

APPENDIX

DEATHS FROM NUPERCAINE

Toxicity of nupercaine clinical

Deaths from spinal injection—
- Hechenbach, W Zteschr f urol. Chir, 28 295 — 010
- Jones, W H Quoted by Arnheim and Mage, Lancet, 1930, 219 540 — 0075
- Steinbruck, M Zentralbl f Chir, 1930, 57 273 — 014
- Arnheim and Mage (Weinstein) Surg, Gynec & Obst, 1932, 54 826, 2 c cm of 1 200 — 010
- Keyes and McLennan Am J Surg, 1930, 60 1 — 010
- Idem, J Am M Ass, 1931, 96 2085 — 010
- Ibid — 010
- Ibid — not stated

Deaths from intraperitoneal injection—
- Mandl, F Zentralbl f Chir, 1930, 57 2966 — 150 c cm of 1 1000
- Idem Wien klin Wchnschr, 1929, 42 1393

Deaths from topical application—

Nose—
- Muenchen med Wchnschr, 1929, 76 2009

Urethra—
- Tinnin, F Samml Vergiftungsfallen, 1932, 3 215 — 10 c cm of 1 5 per cent

Bladder—
- Keyes and McLennan. Am J Surg, 1930, 9 1 — amount not stated

Infiltration—
- Freund Klin Wchnschr, 1929, 8 1444 — 130 c cm of 1 1000

Kuchael. Ugesk. f. Læger 1931 37 924
110 c. cm of 1:1000
Delagrand Ugesk. f Læger 1931 411 1006
120 c cm of 1 000
Seibert Quoted by Keyes and McLennan (loc cit)
Chirurg, 1929, 1 1113 90 c cm of 1 1000
New and Non-official Remedies, 1937 p 53
135 c. cm of 1 1000
Medico-Legal. J Am M Ass 1933, 100 45
1 1500
Hirschfelder and Bieter Physiol Rev 1932, 12 136
15 c cm. of 1 per cent
Keyes and McLennan Am J Surg, 1930, 9 1
350 c. cm of 1 1000
Ibid not stated 1 per cent (by mistake)
Ibid not stated 10 per cent (by mistake)
Ibid 80 c. cm of 1 per cent (by mistake)
Idem J Am M Ass 1931 96 2086
20 c cm of 2 per cent

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A NOTE ON PRIMARY SHOCK

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THE proper evaluation of the several etiological factors commonly thought to underlie primary shock is of considerable clinical importance The interrelation of these factors has been discussed too frequently to warrant recapitulation here For a recent summary of the subject the reader referred to an article by Walter Cannon It seemed that one bit of evidence might be obtained from a study of the systemic effects of local tissue damage in an animal isolated, physiologically, from the traumatized tissues

The literature upon parabiosis, vascular parabiosis, and crossed circulation was reviewed, beginning with Paul Bert's account of his *greffe animale* No record was found of a satisfactory application of these to the study of shock

Vaccarezza, in a study directed toward reaching a better understanding of the effects of tissue injury of several sorts, performed the following experiments, using dogs as experimental animals and chlorasol for anesthesia In a series of experiments, the skin of one leg, from claws to "two finger breadths above the femorotibial articulation" was subjected to thermal injury The result was physiological collapse and death within 10 hours Then, by leaving intact the nerves to the extremity and clamping the vessels supplying and draining it, he was able to mitigate these effects Finally, he established a vascular union between two subjects in such a fashion that blood perfusing the traumatized extremity of one animal was returned to the systemic circulation of the other The technique was as follows after treating the leg of one animal, A, Vaccarezza injected physiological salt solution through the femoral artery until it was returned clear via the corresponding femoral vein An anastomosis was then carried out between this femoral artery and the carotid artery of a normal animal, B In this way blood from the uninjured animal B irrigated the leg of A Since the femoral nerve was left intact, the injured extremity had nervous connection with animal A and vascular connections with the healthy animal B In the two experiments performed, the uninjured animals died, in 5 and 8 hours, while the traumatized animal lived It was noted that the circulatory exchange persisted only "a few hours," due to the fact that blood coagulated and occluded the anastomoses

The evidence from these experiments contributed to the author's conclusion that "the cause of shock and death in these cases is due exclusively to the influence of toxic products which, originating at the site of trauma, are carried by blood vessels and lymphatics to the general circulation "

Several criticisms of the foregoing suggest themselves In the first place, the experiments were not controlled The history of crossed circulation experiments suggests that evidence thus obtained must be based upon carefully controlled conditions The thromboses that occurred at the anastomoses in addition to terminating the experiments for all practical purposes, indicate the existence of another pathological process, in itself capable of producing death through embolism In addition, death may follow anesthesia alone, or, as we later found, may occur from pulmonary lesions incident to the prolonged immobilization under anesthesia Finally, the absence of necropsy reports leaves one somewhat in doubt as to the actual causes of death

Since the findings have been quoted by other investigators in spite of these possible objections, and inasmuch as they seemed a particularly pertinent contribution, we decided to repeat and extend the work

EXPERIMENTAL PROCEDURE

Large animals were selected and paired for equality of weight With one exception,

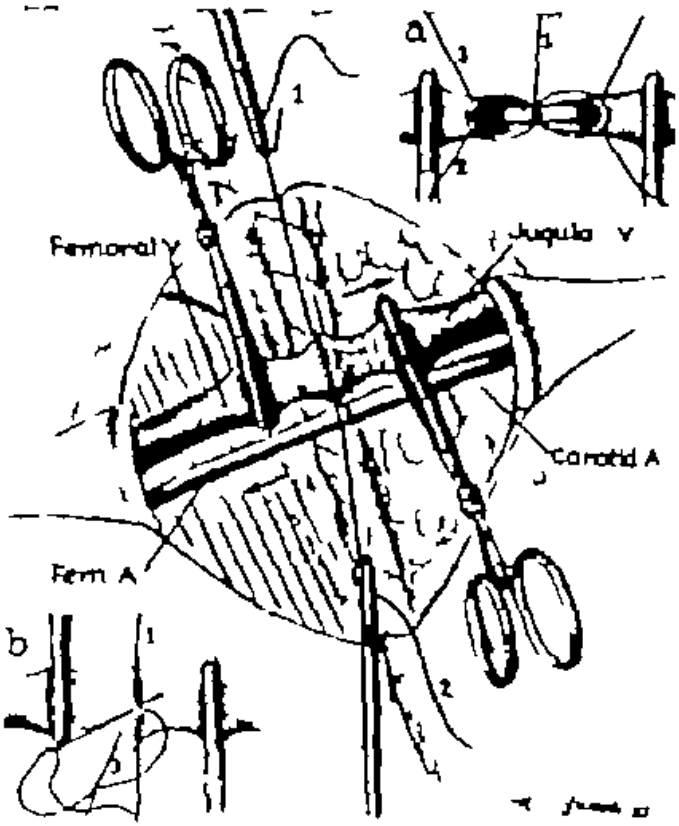

Fig 1 Details of the operative procedure used in experiments 1, 2 and 4, and in controls The anastomoses, a, b, follow the familiar Doerfler Carrel-Guthrie technique. The posterior wound edges have been united

the extremity of the heavier subject was used.

After preparation of the left hind leg and thigh of one animal A and the neck of the other animal B each animal was given an intravenous injection of 0.5 gram of sodium amytal in 10 per cent solution. The skin was prepared with iodine and alcohol, and the adjacent skin surfaces posterior to the sites of incision were brought together with a continuous suture. Small amounts of ether were administered from this point to the completion of the operation. It should be stated definitely at this point that anesthesia was complete and effective throughout all experiments

An incision was made to the left of the midline of the neck of animal B and through this the jugular vein and common carotid artery were exposed and liberated from surrounding tissues. These then were coated with sterile mineral oil, returned to their beds, and lightly covered with gauze moistened with warm physiological salt solution.

A left inguinal incision served to expose the proximal ends of the femoral artery and vein of animal A. Branches of the artery and tributaries to the vein in this region were ligated to avoid the possibility of a vascular "shunt," and the vessels were freed from surrounding tissues, the femoral nerve being carefully protected The vessels were then coated with mineral oil and overlaid with moist sponges. A continuous silk suture was employed to bring together the posterior portions of both wounds

The leg of animal A was then treated from the claws to points 4 centimeters above the femorotibial articulation anteriorly and 6 centimeters above this articulation posteriorly the Vaccarezza technique being used Next, the femoral artery and vein of animal A were divided high in the groin between clamps. By means of a bulb syringe with a drawn out and rounded tip, the vascular bed of the extremity was washed out rapidly with warm salt solution the injection being made under moderate pressure into the artery and continuing until only bloodtinged solution came from the free end of the vein. These vessels were caught gently in rubbershod clamps, lubricated and protected by moistened gauze while the carotid and jugular vessels of animal B were divided high in the neck

The anastomoses were then carried out, the carotid artery of animal B being united with the femoral artery of animal A, and the femoral vein of animal A with the jugular of animal B so that blood leaving the systemic circulation of animal B traversed the vascular channels of the leg of animal A and returned to its original source.

The operative procedure and the method used in the anastomoses are illustrated in Figure 1 The unions were accomplished by the familiar Doerfler-Carrel-Guthrie technique in which, after the placing of three "guy" sutures (Figure 1a) a continuous suture of fine, lubricated silk, piercing all coats, is employed to bring the edges into end-on approximation (Figure 1b) The drawing also shows the anastomoses running in front of the suture line uniting the posterior portions of the two incisions. Upon completion of the anastomoses, this suture was continued

TABLE I

Maneuver	11 Controls 12		13 Experiments 14	
Weight of A	2 9 k	29 1 k	2 7 k	22 6 k
Weight of B	22 5 k	23 1 k	2 7 k	7 k
Anesthetic	00	00	00	.00
Operation	.40	35	1 00	1 00
Trauma	None	None	00	2 15
Anastomoses functioning	2 55	2 50	3 5	3 30
Division	1 10	12 05	12 05	11 50
Fate of A	Recovery	Recovery	Killed	Killed
Fate of B	Recovery	Recovery	Recovery	Recovery

The salient data of the two experiments on thermal trauma (Nos 13 and 14) and the two control procedures (Nos 11 and 12) Time intervals are given in minutes and hours, the experiments being presumed to begin with the administration of the anesthetic.

in such a fashion as to unite the skin edges of the two wounds entirely around the vessels—a tube effect

With the completion of the operation, ether was discontinued animal B was rolled toward animal A, and the two turned completely over This, as will be seen, was found an important part of the technique Care was taken to support the head of animal B in such a manner that there could be no interference with the circulation of the leg of animal A Other precautions were taken to this same end In all experiments, this leg remained warm, and phenolsulphonphthalein, injected intramuscularly into animal A, was found in quantity in the urine of animal B

It was planned to terminate the experiments after 8 hours, this period equaling the longest survival of animal B in Vaccarezza's experiments However, the anastomoses actually functioned 8 hours and 40 minutes and 8 hours and 25 minutes in the 2 experiments The animals were given continuous nursing attention Small doses of morphia and rare whiffs of ether sufficed to keep them soundly asleep

At the conclusion of the experiments, the anastomoses were examined (on the "A" side of the arterial union and "B" side of the venous) by inspection, palpation, filling tests, and finally by escape of blood "beyond" the points of union In every case the anas-

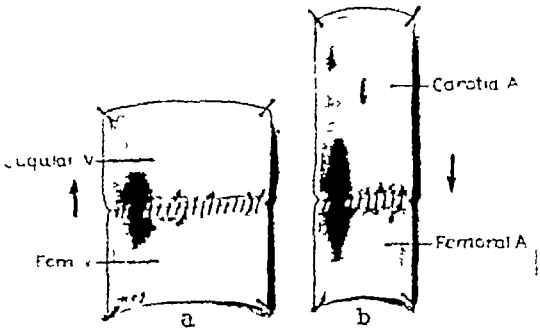

Fig 2 The carotid femoral and jugular-femoral anastomoses from experiment 14 after 8 hours of function This situation accurately represents those found in examinations of the other suture anastomoses Natural size

tomoses were found to be functioning competently After tying the vessels and removing the connecting portions for examination, animal A was killed The wound of animal B was sutured in layers with fine silk, and this animal was returned to its cage

In the two experiments the B animals recovered promptly

There was no wound infection The condition of the opened vessels shown in Figure 2, a drawing from the specimens in experiment 14, was typical of the group

In the two control experiments the anesthesia and operative procedures were identical with the above Both animals in each set of partners survived The anastomoses functioned briskly, and the same examination tested their freedom from thrombosis At the conclusion of these procedures the A animals were not killed The wounds of both partners in the crossed circulation preparation were sutured with fine silk, and the 4 recovered promptly, without infection or other untoward sequelæ These experiments were terminated in each case after the anastomoses had functioned 9 hours and 15 minutes Table I presents the essential data of the foregoing

In two additional experiments the leg of animal A was subjected to mechanical trauma produced by blows with a blunt instrument, under full anesthesia This was carried out rapidly and vigorously, and the

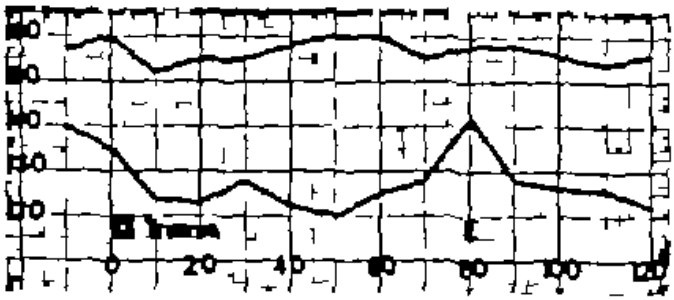

Fig. 3. Graphs of systolic blood pressures in experiments 5 and 16, in millimeters of mercury. Time is in minutes. The elevation at *E* was quite apparently due to a short period of administration of ether. Pulse rates rose very gradually from 120 a minute to 152, and from 121 to 150 in experiments 5 and 16, respectively, during this experimental period.

subsequent very marked edema of the tissues suggested that it had been effective. Because the experiments were of shorter duration, and because earlier effects were anticipated, several minor changes in technique were introduced. Intraperitoneal pentobarbital sodium (50 milligrams a kilogram) was used for anesthesia; anastomoses were carried out preceding the traumatization. Payr cannulas were used in effecting the anastomoses. Continuous blood pressure records of animal B were made, the cannula being inserted into the femoral artery. The experiments were allowed to continue 2 hours after traumatization. In other respects the technique of the two groups of experiments was the same.

Anastomoses were functioning competently at the termination of the experiments, according to the criteria herein given, and phenolsulphonphthalein injected intramuscularly into the leg of animal A following injury appeared in quantity in the urine of animal B. At the end of the experiments the A animals were killed; the B animals were returned to their cages.

The blood pressure levels of the B animals showed a slight decline during and shortly after trauma, possibly due to loss of blood into the vascular bed and tissues of the leg of the A animals. Thereafter the blood pressures returned to relatively high levels in both experiments, where, with minor fluctuations, they remained. The pulse rates rose very gradually from 120 a minute to 152 in experiment 15 and from 121 to 150 in experiment 16. Neither B animal showed other

TABLE II

Measure	5	Experiment	16
Weight of A	[illegible]		[illegible]
Weight of B	[illegible]		[illegible]
Anesthetic	[illegible]		[illegible]
Operation	[illegible]		[illegible]
Anastomoses functioning	[illegible]		[illegible]
Trauma	[illegible]		[illegible]
P S P	[illegible]		[illegible]
Termination	[illegible]		[illegible]
Fate of A	Killed		Killed
Fate of B	Recovery		Recovery

Significant data of experiments 5 and 16 on traumatic shock. Time intervals are as in Table I. *P S P indicates injection of phenolsulphonphthalein.

evidence of primary shock. Both recovered, and 24 hours later gave no obvious evidence of secondary shock. The essential data of these experiments are given in Table II and graphs of the blood pressure levels are given in Figure 3.

METHOD

Considerable difficulty was experienced before we were satisfied with the method—enough to make us somewhat skeptical of the results in Vaccarezza's two uncontrolled procedures. Ten preliminary experiments, with and without traumatization, were carried out. Though the results in these did not weaken the final experimental conclusions, they showed that deaths may be expected from pulmonary lesions presumably incident to the long immobilization and from some anesthetic agents when used for protracted periods. We found two points in technique worthy of observation. In regard to anesthesia, when using sodium amytal intravenously in experiments of this duration it seems best to use an amount sufficient only for introductory narcosis, and to use morphia and ether for subsequent anesthesia; pentobarbital sodium probably is more satisfactory than sodium amytal. Second, immobilization in one position should be limited to periods of 4 hours.

Several general remarks based upon our review of parabiosis, vascular parabiosis, and

crossed circulation may be in order Though the technique of parabiosis is the easiest of the three to carry out, the method has other pitfalls Conclusions, to be convincing, should be based upon a number of experiments When the time element is introduced, the relationship of the significant maneuver should be cleared of all doubt For, as Dragstedt and others have pointed out, unexplained deaths, not associated with characteristic lesions and quite unpredictable, are not uncommon

The crossed circulation techniques are more difficult to carry out and require, on the part of the experimenter, a very clear concept of the problem in hand Some of the experiments noted so far departed from the comparison to the physiological state that analogies drawn from them are of doubtful validity Doubt surrounds other results because of the failure of the authors to offer evidence that circulation was in progress during the experiment Finally, in at least 2 cases, adaptations of the method were used which were far too crude to justify significant conclusions

In general, we feel that parabiosis is best adapted to the study of effects that are relatively subtle, that are progressive, and that take place over a period of days or weeks Vascular parabiosis and crossed circulation, on the other hand, seem best adapted to experiments of short duration in which relatively gross changes are anticipated

CONCLUSION

Two varieties of trauma affecting the leg of one animal perfused by the blood of a second failed to evoke evidence of shock in the second animal This result tends to derogate the postulate that a lethal toxin is formed in traumatized tissues

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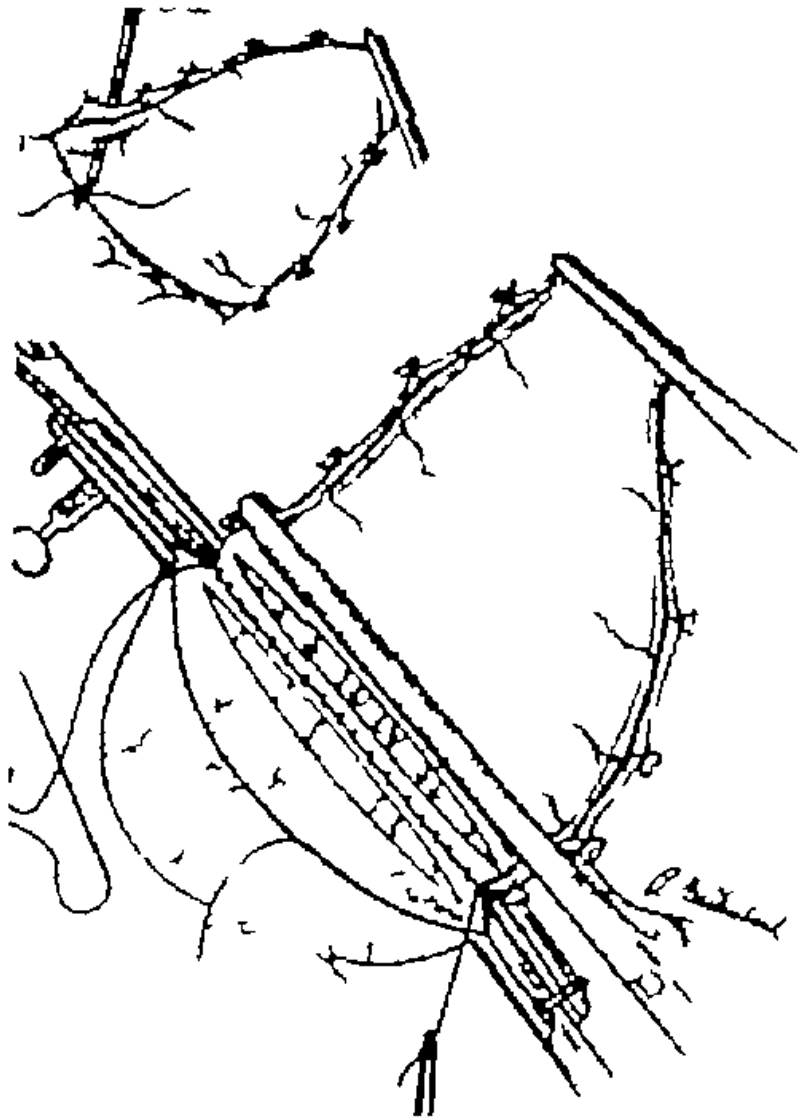

Fig. 5. The insert shows the stomach pulled downward and deflected over the left costal arch so as to expose the left gastric artery which is ligated and cut. The stomach and jejunum are fixed in position by two Lane intestinal clamps, and continuous catgut serosomuscular sutures unite the posterior wall of the stomach to the jejunum. The serosa and muscularis of the posterior wall of the stomach are cut and the vessels in the submucosa are ligated.

CLINICAL SURGERY

FROM THE DEPARTMENT OF SURGERY, NORTHWESTERN UNIVERSITY

TECHNIQUE OF GASTRECTOMY

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GASTRIC resection today offers the only curative procedure for malignancies of the stomach Although, theoretically, total extirpation of the stomach is probably the operation of choice, this procedure is associated with too high a mortality to be of practical value Subtotal gastric resection with the removal of the greatest possible portion of the stomach and of the surrounding tissue, such as the lesser and gastrocolic omentums and the lymph glands in these structures, gives the best results In the advanced cases, in which the malignancy has invaded the liver, transverse mesocolon, transverse colon, anterior abdominal wall and pancreas, gastric resection is only a palliative procedure, it removes an ulcerating, bleeding, or obstructing tumor, relieves pain, but does not give a permanent cure or appreciably lengthen life

There are many types of gastric resection, the descriptions of which are beyond the scope of this paper The operation that has given us the best results is the Pólya modification of the Billroth II The technique of the Billroth II, as carried out in our practice, will be discussed and the pre-operative and postoperative care briefly summarized

PRE-OPERATIVE TREATMENT

The amount of pre-operative treatment depends upon the general condition of the patient and the type of gastric malignancy From the point of view of pre-operative management, the gastric lesions may be divided into two groups (1) stenosing tumors which produce pyloric obstruction and gastrectasis, (2) tumors which do not produce obstruction The stenosing tumors lead to a gastric dilatation, retention of food, hypertrophy, and edema of the gastric wall These effects of the obstruction can be overcome by lavage of the stomach to free it of food residue and by constant aspiration through a Levine tube for several days During this period the patient's water balance is maintained by the daily administration of 3,000 to 4,000 cubic centimeters of 5 per cent dextrose in Hartmann's solution, by intravenous drip The non-obstructing tumors do not lead to these stomach changes and do not require this gastric decompression Patients are allowed liberal amounts of high carbohydrate, non-residue foods and a large amount of liquids If a marked anemia is present, blood transfusions are indicated before operation

ANESTHESIA

The choice of anesthesia in patients with gastric malignancies, especially if associated with loss of weight and debility, is of importance Patients who are in fair general condition are given a combination anesthesia of avertin (tribrom-ethenol) in doses of 70 to 80 milligrams per kilogram body weight, supplemented by ethylene or 1 per cent novocain local infiltration Emaciated patients with possible kidney damage are better operated upon under morphine-scopolamine analgesia and local infiltration of 1 per cent novocain and supplemented with ethylene when necessary

OPERATIVE TECHNIQUE

The operative technique for gastrectomy may be divided into various steps, such as (1) abdominal incision, (2) determination of operability, (3) mobilization of stomach, (4) gastro-intestinal anastomosis

The abdominal incision most suitable for gastrectomy is the left paramedian incision However, if the lesion is located high on the fundus or cardia of the stomach, the exposure through this incision may be inadequate In these cases the operation is facilitated by enlarging the paramedian incision with a transverse incision across the left rectus and extending to the lateral abdominal muscles

Fig. 1. The index and middle fingers are inserted through an opening in the gastrohepatic omentum and by blunt dissection separate the posterior wall of the stomach from the transverse mesocolon.

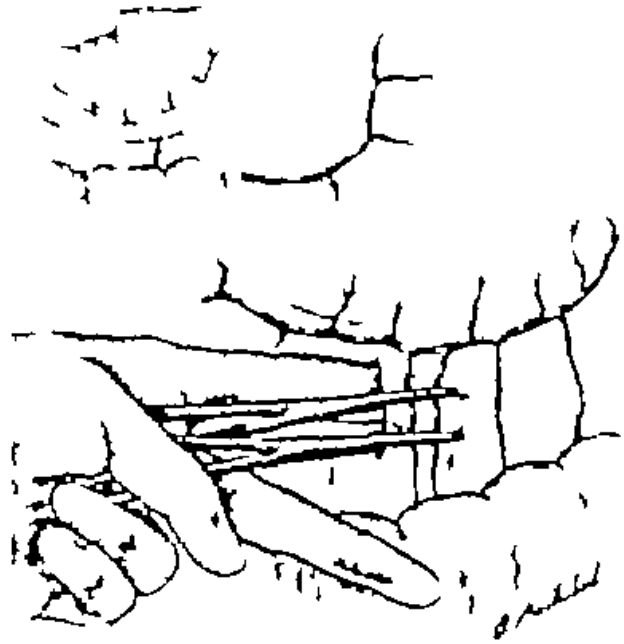

Fig. 2. The gastrocolic omentum is cut between clamps and ligated. The fingers of the left hand separate the gastrocolic omentum from the mesocolon.

Once the abdomen is opened the first factor to determine is operability. If the lesion is not adherent to the anterior abdominal wall, liver or pancreas, the stomach and transverse colon are lifted up and examined for adhesions between the stomach and transverse colon or transverse mesocolon. If the transverse mesocolon is invaded by the tumor, the involvement of the middle colic artery is determined. If this artery can be spared, the mesocolon can be resected with the stomach without interfering with the blood supply of the transverse colon. An opening is made in the gastrocolic and gastrohepatic omentums and the posterior surface of the stomach is inspected for adhesions to the mesenteric vessels, transverse mesocolon and pancreas. If the tumor extends toward the right, the right lobe of the liver is drawn aside and the gall bladder, common duct, and surrounding structures are explored. If the lesion is limited to the stomach and there are no metastases or extension of the malignancy to the surrounding structures, resection may offer a cure. If there is local extension of the mass or metastases to the regional lymph glands, resection is palliative.

If the lesion is resectable, the first step in the technique is mobilization of the stomach. This is accomplished by inserting the index and middle fingers of the left hand through an opening in the gastrohepatic omentum and by blunt dissection separating the posterior wall of the stomach from the transverse mesocolon (Fig. 1). The gastrocolic omentum is then divided between forceps (Fig. 2) and doubly ligated. If the lymph glands are involved, the ligation is done as close as possible to the transverse colon. The division of the gastrocolic omentum is first done toward the cardia and continued toward the pylorus. In the region of the antrum, the gastrocolic omentum is adherent to the mesocolon and can be separated by blunt and sharp dissection, care being taken not to injure the vessels of the mesocolon, especially the middle colic artery. If the lesion has invaded the mesocolon and separation is impossible, the diseased portion of mesocolon must be excised. If the middle colic artery is injured, the adjoining colon must be resected with the stomach. As the separation approaches the pylorus, two peritoneal folds are seen passing from the hepatic flexure of the colon to the duodenum and pylorus, one passing to the right and one to the left. The right fold contains the right epiploic artery and vein which are severed between forceps and ligated. The left fold leads to the pancreas and contains many small branches of the gastroduodenal artery and vein. These vessels, although they are small in size, are cut between forceps and doubly ligated. By this procedure the duodenum is gradually freed from the head of the pancreas.

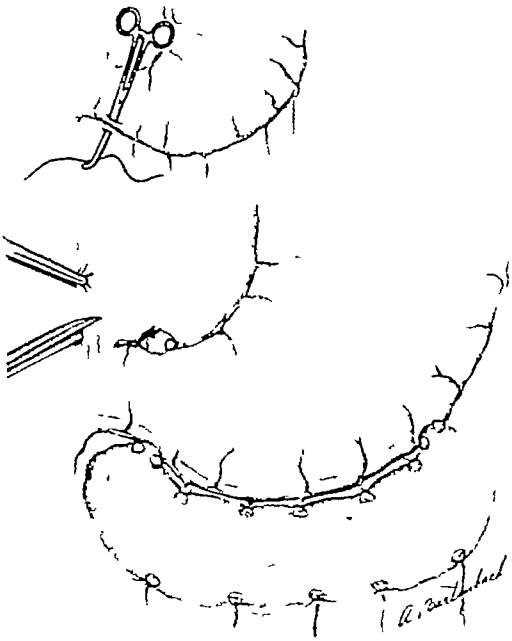

Fig 3 The gastrocolic omentum is cut and the vessels ligated The gastro epiploic and pyloric (right gastric) arteries are ligated and cut

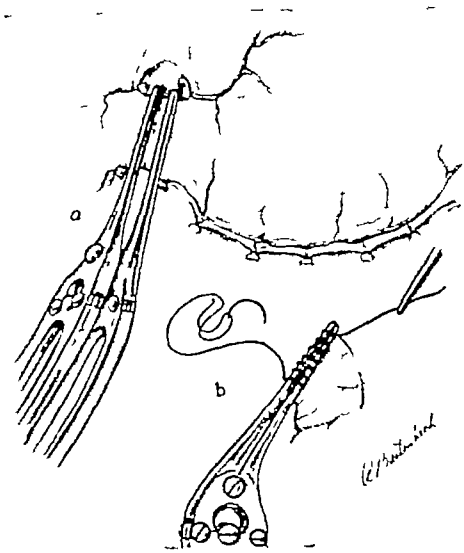

Fig 4 Two Payr clamps are placed close to each other in the first portion of the duodenum and the bowel cut between them The duodenal stump is closed by a continuous basting suture running over the Payr clamp As the clamp is removed the suture is pulled taut and inverts the crushed end of the duodenum

The next step in the mobilization of the stomach is division of the gastrohepatic omentum The stomach is now brought down and to the left so as to bring the duodenum and lesser omentum into view Beginning at the opening in the gastrohepatic omentum through which the fingers were placed to mobilize the posterior surface of the stomach, the gastrohepatic omentum is cut between forceps and ligated This mobilization is carried downward toward the duodenum In the hepatoduodenal ligament there are many small vessels which are carefully isolated, cut between forceps, and ligated After the duodenum is mobilized, it is divided between two Payr clamps (Fig 4), care being taken to protect the surrounding tissues from contamination The proximal stump of duodenum is covered with a lap sponge and the distal stump is closed Closure of the duodenal stump is an important step in the procedure of gastrectomy and failure of adequate closure has resulted in many unfortunate postoperative sequelæ The stump is closed by a continuous silk suture which, beginning at one end, grasps a fold of serosa and muscularis on one side a short distance below the forceps, then the suture is carried over the forceps and a similar stitch is taken on the other side of the duodenum and then back over the forceps to take a stitch on the first side and so on until the other end is reached As an assistant slowly removes the clamp, the operator pulls the two ends of the suture taut This procedure closes and folds in the cut edges of the duodenum Without tying the ends of the suture, the operator places an interrupted Lembert suture at each end of the duodenal stump and the free ends of the continuous suture are then tied to the Lembert suture A row of interrupted Lembert sutures are placed over the first suture line The suture line may be further reinforced by a third layer of interrupted Lembert sutures or by covering it with omentum or capsule of the pancreas

Further mobilization of the stomach is accomplished by dividing the gastrohepatic omentum toward the cardia The stomach and duodenum are pulled downward so as to stretch the attachment of the gastrohepatic omentum to the lesser curvature At a point close to the gastric border the omentum is cut between forceps and doubly ligated, applying two ligatures on the side toward the cardia on account of the tendency of the vessels in the fatty infiltrated omentum to slip The branches of the coronary artery which radiate from the gastrohepatic omentum to the anterior and posterior walls of the stomach are cut between forceps and ligated During this

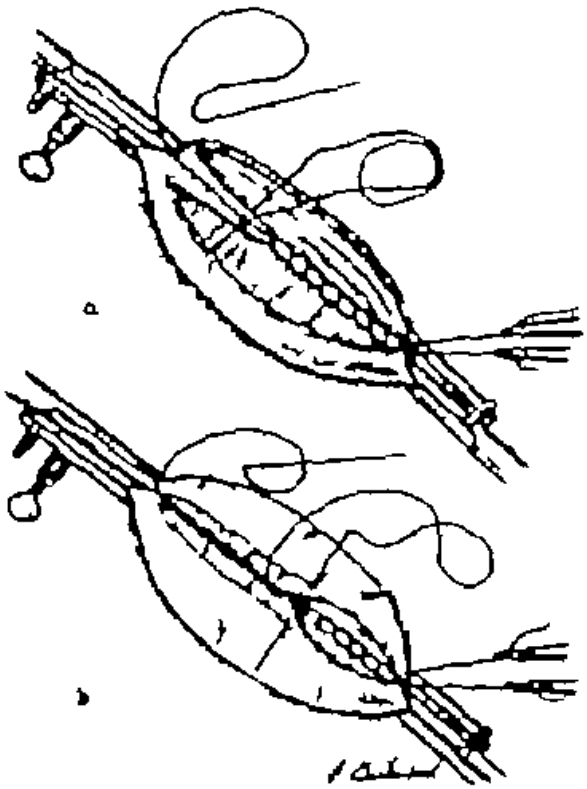

Fig. 6 a, The stomach is amputated and a continuous catgut suture passes through all the layers of the stomach and jejunum uniting the posterior wall of the stomach to the jejunum. b As the suture reaches the lesser curvature it is carried over to the anterior wall as a continuous suture through the mucosa At the greater curvature the suture is tied to its short end

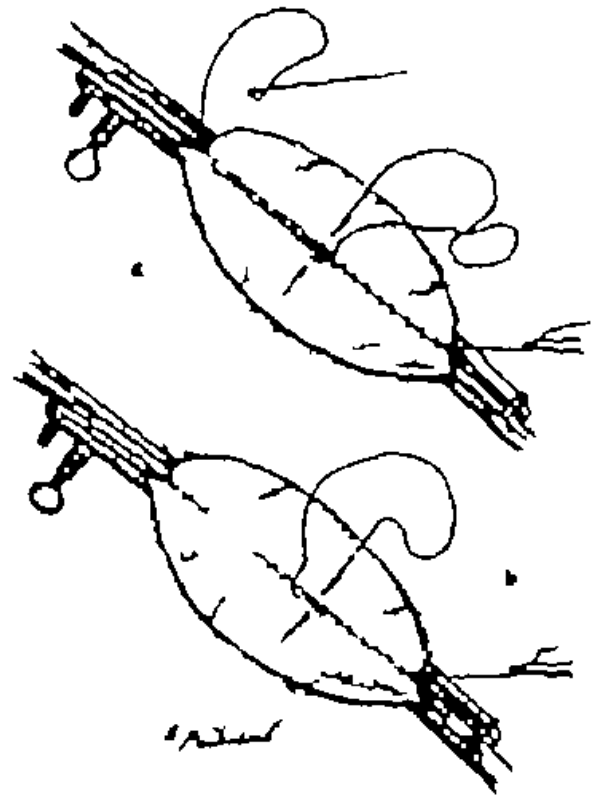

Fig 7 a, The mucosal suture described in Figure 6 is continued both as a continuous seromuscular suture and tied to the seromuscular suture of the posterior wall and cut, leaving the posterior suture intact b, The posterior seromuscular suture is continued over the anterior portion of the anastomosis as a third layer suture.

procedure the lesser curvature of the stomach is freed of its peritoneal covering The stomach is now lifted up and turned back over the left costal arch so that the posterior surface may be inspected. The gastrosplenic ligament, vasa brevia arteries, and adhesions are cut between forceps and ligated

The fourth step in the procedure of gastrectomy is the performance of the gastrojejunal anastomosis. The stomach which has been extensively mobilized, is brought down from beneath the costal arch and grasped with a Lane intestinal clamp as high as possible above the tumor and the redundant stomach reflected over the left costal arch so as to make the posterior surface easily accessible. The first loop of jejunum is brought through an opening in the transverse mesocolon, and is approximated to the posterior wall of the stomach so that it runs from lesser to greater curvature in an antiperistaltic direction (Fig. 5, opposite p. 611) The segment of jejunum between the stomach and duodenojejunal angle is made as short as possible without causing too much traction on the suture line A second Lane intestinal clamp is applied to the jejunum which is approximated to the posterior wall of the stomach and the forceps are fixed in position. The jejunum is attached to the posterior wall by a continuous Lembert catgut suture. After the completion of this suture the distal segment of stomach is clamped and amputated about 1 centimeter from the Lembert suture The jejunum is then opened about 0.5 centimeter from the Lembert suture. The cut edges of the posterior wall of the stomach and jejunum are sutured with a continuous over and over suture grasping all three layers, (Fig. 6) This suture is started at the greater curvature and progresses toward the lesser curvature. When the anterior wall is reached, instead of grasping all three layers, only the mucosa is sutured along the anterior wall. When the greater curvature is reached, the ligature is tied to the short end, and is then reversed, grasping the serosa and muscularis of the anterior wall of the stomach and jejunum (Fig 7) When the lesser curvature is reached, this ligature is tied to the continuous seromuscular suture of the posterior wall and is then cut, leaving the posterior suture

with its attached needle intact The clamps are now removed Following this, the posterior seromuscular suture is continued along the anterior wall as a third layer suture The entire suture line is reinforced with interrupted silk Lembert sutures Along the lesser curvature of the stomach where the stomach has been freed from its peritoneal covering, the anterior and posterior walls are approximated by interrupted Lembert sutures, thereby burying the deperitonealized area of the lesser curvature

The suture line is now drawn through the opening in the mesocolon (Fig 8) The stomach is attached by interrupted Lembert suture to the edges of the opening in the mesocolon If the remaining stomach is short, it may be impossible to pull it down through the opening in the mesocolon In these cases, the opening may be closed around the loops of jejunum

The abdominal incision is closed without drainage of the peritoneal cavity The incision is closed with interrupted sutures in three layers Catgut is usually used in the posterior sheath of rectus, transversalis fascia, and peritoneum which are taken as one layer and in the anterior rectus fascia Interrupted silkworm is used in the skin In debilitated patients with poor healing properties, interrupted silk sutures may be used throughout all layers

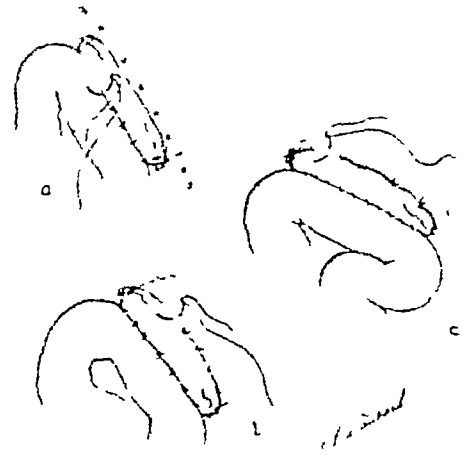

Fig 8 a, The anastomosis is reinforced with a layer of interrupted Lembert sutures b The posterior wall of the stomach is sutured to the mesocolon by interrupted sutures c The anterior wall of the stomach is sutured to the mesocolon

POSTOPERATIVE TREATMENT

Immediately after the operation a blood transfusion is given Following this, transfusions of blood are repeated as conditions warrant During the first 4 or 5 days, the stomach is kept decompressed with a Levine tube and constant suction During this period the water balance is maintained by the administration of 3,000 to 4,000 cubic centimeters daily of 5 per cent dextrose in Hartmann's solution About the fifth or sixth day the Levine tube is clamped off and fluids are given orally If the fluids are tolerated, the Levine tube is removed and the diet is gradually increased

The general postoperative care is essentially the same as that of any laparotomy patient He is encouraged to change position in bed and to sit in a semi-recumbent position in order to avoid pulmonary complications

Patients with a malignancy have poor healing properties so that it has been our practice not to remove the tension sutures of the abdominal incision for at least 2 weeks, and, if the patient is emaciated, they are left in as long as 3 weeks Many eviscerations may possibly be avoided by using this precaution

RETRO-ESOPHAGEAL GOITER

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RETRO-ESOPHAGEAL goiter while not a surgical rarity is sufficiently unusual to warrant a report of 4 cases. The object of this discussion is, first, to place on record these case histories and, second, to show that this anatomical variant of goiter constitutes a definite clinical entity which, with the aid of a few simple laboratory examinations, may be accurately diagnosed before operation.

It has not been an uncommon experience, especially with adenomatous goiters, to find at operation, small projections of thyroid tissue lying in the tracheo-esophageal groove, or in the cleft between the esophagus and the vertebral column. Failure to visualize these masses, due to incomplete delivery of the thyroid lobe, is undoubtedly responsible for the many so called "recurrences" following thyroidectomy for adenomatous goiter. However, it is not this variant of goiter to which I refer in this paper. The variety encountered in the following cases has passed, in its growth, medially from the postero-internal aspect of the thyroid lobe across the midline between the pre-vertebral fascia and the posterior surface of the esophagus.

It is probable that the factor influencing the growth of retro-esophageal goiter is similar to that which determines the development of a substernal goiter: the direction of growth is in the line of least resistance. In the initial enlargement of the gland, the greatest bulging usually occurs anteriorly and laterally. However, after the goiter has become large, the pretracheal muscles become more or less unyielding and further growth may occur in the direction of least resistance, either substernally or along the fascial plane behind the esophagus. As Pemberton points out, the relative greater frequency with which retro-esophageal goiters are encountered in secondary operations for recurrent disease may be explained by the fact that the tissues anteriorly and laterally are unyielding because of the presence of scar tissue. However, it seems more likely that in the so called recurrent cases, these projections do not develop subsequent to operation but were overlooked by the surgeon who failed to dislocate the thyroid lobe completely. The absence of adhesions and the ease of delivery of the retro-esophageal projection, in one of the described cases, would seem to corroborate this viewpoint.

A well defined retro-esophageal goiter will invariably cause symptoms which, if carefully analyzed, will be found to be out of all proportion to any obvious anterior and lateral thyroid enlargement that may be present. In our 4 cases herewith reported, all complained of attacks of choking brought on especially when turning the head to the side opposite to the point of entrance of the goiter in the retro-esophageal space. This was more evident with the patient in the reclining position. One patient developed attacks of dyspnea which were relieved by inclining the head toward the affected side. This was corroborated by the findings at operation. One patient complained of frequent spells of coughing which came on invariably after retiring at night. Assuming an upright position often brought relief. A sense of constriction in the neck was noted by all the patients. One patient complained of difficulty in swallowing which, however, was not constant. In 1 instance the overlooked retro-esophageal extension was a factor in the continuation of severe thyrotoxic symptoms. The outstanding symptom in 2 instances was hoarseness which was variable in intensity and duration. The most recent patient disclosed a paralysis of the right vocal cord on the same side of entrance of the retro-esophageal goiter.

It may be extremely difficult to make a diagnosis of retro-esophageal goiter on the basis of physical signs alone. If the antetracheal portion of the goiter is definitely enlarged, a clinical diagnosis may be impossible. If the thyroid lesion is insignificant, the finding of anterior displacement of the trachea, especially against the upper manubrial edge, should cause the surgeon to suspect a retro-esophageal extension. In the most recent case it was possible to palpate the trachea pushed forward by a large adenoma, which could be moved from left to right behind the esophagus. In 1 of the 4 cases, the abnormality was not suspected before operation. In the 3 remaining instances, the retro-esophageal position of the goiter was diagnosed clinically.

In attempting to seek a more graphic method of depicting the presence of a retro-esophageal goiter before operation and to fortify the clinical diagnosis by some exact method, in 1933 I had a lateral roentgenogram of the neck made on the third case reported here. This film indicated a

well defined anterior displacement of the trachea Then, in order to outline the position of the esophagus in relation to the trachea the goiter and the vertebral column another lateral roentgenogram was made at the moment of swallowing a mouthful of barium This clearly delineated the displacement of the esophagus by a mass behind its posterior surface The X-ray films of the fourth case, (Fig 5), disclosed in addition, a narrowing of the upper esophagus by the posteriorly placed adenoma I believe that these 2 methods of X-ray examination are valuable aids to the surgeon in arriving at a pre operative diagnosis of retro-esophageal goiter

At operation removal of the retro esophageal projection may offer little difficulty If this portion of the goiter is large the danger of injuring the recurrent laryngeal nerve is real In 2 of the reported cases, it was possible to roll out the posterior projection while dislocating the major portion of the lateral lobe and to remove it with the remainder of the goiter In the 2 other cases this maneuver was impossible Realizing the danger of recurrent nerve injury, I resected the major part of the lateral lobe leaving the retro esophageal portion *in situ* All severed vessels were then tied so as to free the operative field of clamps A temporary ligature was then placed about the inferior thyroid vessels in order to control bleeding from its branches The posterior portion of the goiter was then dissected out of its bed in a practically bloodless field, without endangering the integrity of the recurrent nerve or parathyroid bodies

CASE REPORTS

CASE 1 Mrs L H, aged 53 years, was first seen on November 15 1928 She complained of a goiter of 20 years standing with recent increase in size, especially on the right side For the preceding 4 years, she had noted increasing nervousness palpitation and a loss of 30 pounds in weight She also complained of choking sensations which were aggravated by turning the head toward the left side in a reclining position In addition she had the sensation of constriction about the neck

Examination showed an elderly woman quite nervous There was no exophthalmos There was moderate dental caries The heart was somewhat enlarged to the left and was totally irregular Pulse deficit amounted to 20 Pulse rate was 160 Blood pressure, systolic 170 diastolic 90 Laryngeal examination was negative She was admitted to the New York Hospital on November 26 1928 Laboratory tests revealed a negative urine, a negative Wassermann, and a normal blood count Basal metabolic rate on November 20, 1928, was plus 83 per cent Following rest in bed, the administration of Lugol's solution, a high caloric diet, etc, the patient's basal metabolic rate dropped to plus 31 per cent within 10 days

Operation was performed on December 14, 1928 Because of the large size of the goiter, the pretracheal muscles were divided transversely There were numerous adenomas some solid, some cystic, extending into the lateral recesses

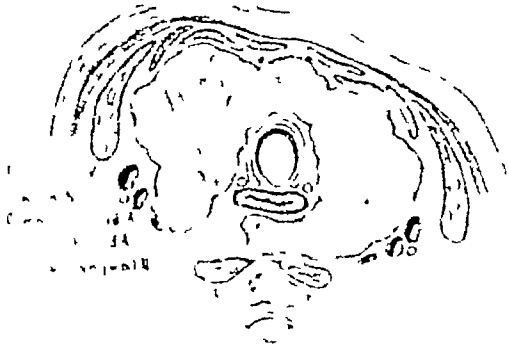

FIG 1 Cross section of the neck showing diagrammatically the retro esophageal extension in Case 1 The relative position of the recurrent nerves and inferior thyroid vessels should be noted

of the neck and partly beneath the sternum Great difficulty was encountered in attempting to dislocate the right lobe It was finally determined that this was due to a large adenoma which passed posteriorly between the esophagus and vertebral column (Fig 1) The right lobe and isthmus were partially resected and the bleeding points were ligated A temporary ligature was then placed around the inferior thyroid vessels and, by a combination of sharp and blunt dissection the retro esophageal mass was finally dislocated into the wound and removed The recurrent laryngeal nerve was never visualized A subtotal resection was then done on the left side, the adenoma which had grown down behind the manubrium, was removed

After operation this patient did well Laryngeal examination on the fourth day after operation was negative The pathological examination of the removed goiter disclosed numerous adenomas with some hyperplasia The patient was discharged with the wound completely healed on the twelfth day after operation The basal metabolic rate was plus 2 per cent She has remained well to date

The follow up on this patient is extremely interesting She developed, 1 year later, signs of an abdominal tumor which upon operation, proved to be actinomycosis of the transverse colon This was reported in the *Annals of Surgery*, 1934, 99 p 531

CASE 2 Mrs H S, aged 30 years, referred by Drs W Klingman and I Hauser was first seen October 2 1933, at which time she complained of a goiter of 6 months' duration She stated that for the preceding year, she had been troubled with a persistent cough which became more evident at night after retiring These coughing spells were productive of a small amount of mucus In addition she experienced frequent attacks of hoarseness which did not respond to therapy and which spontaneously subsided after a day or two For the past 5 or 6 months, she had been conscious of a sense of constriction about the neck The attacks of coughing at night time were relieved when she assumed an upright position In addition, she presented symptoms of mild thyrotoxicosis, palpitation, nervousness dyspnea on exertion, mild exophthalmos, a loss of 5 pounds, and tremor

Examination showed a well developed young woman, troubled with a persistent dry cough The skin was moist. There was slight exophthalmos and the thyroid gland was uniformly enlarged and soft The lateral borders could not

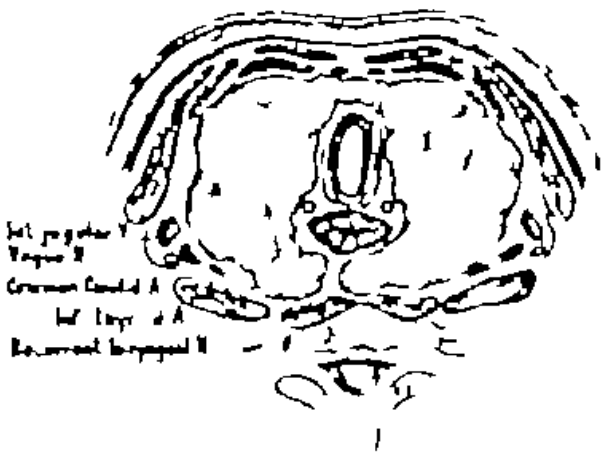

Fig. Cross section of the neck to show bilateral retro-esophageal extensions of the goiter described in Case. The position of the various anatomical structures are indicated.

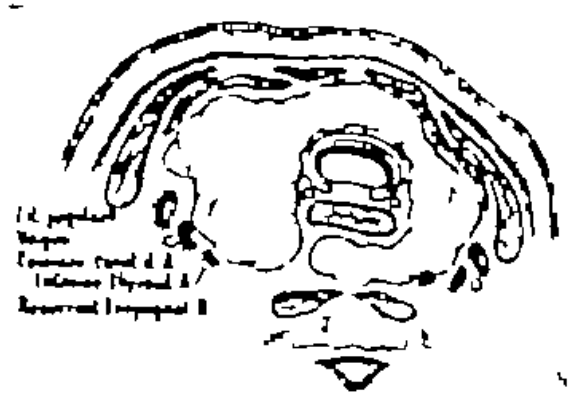

Fig. 3. Cross section of neck. Case 3, showing the retro-esophageal projection of the right lobe of the thyroid which was responsible for persistence of hyperthyroid symptoms in addition to the mechanical effects of the mass.

be definitely demarcated. Laryngeal examination revealed normally functioning vocal cords. The heart was negative. Pulse was 128. Blood pressure was systolic 1 2, and diastolic 84.

She was admitted to the New York Hospital on October 1 933, where further study revealed basal metabolic rate of plus 18 per cent, negative urine, and negative blood examination. An X-ray examination of the chest showed no substernal projection of the goiter. The probability of a retro-esophageal extension of the goiter was suggested before operation.

Operation was performed on October 6, 933. Through the usual collar incision, the thyroid gland was exposed and found to be moderately enlarged. It was filled with numerous small adenomas, varying in size from 1 to 3 centimeters in diameter. The isthmus was divided and an attempt was made to deliver the right lobe. It was soon evident that there was present, a projection of thyroid tissue posteriorly between the esophagus and vertebral column. A finger inserted into this groove met resistance on the left side. It was found that the left lobe also presented an extension posteriorly which almost met the right sided projection behind the esophagus (Fig.). It was possible in this case to enucleate the projection on each side and to perform subtotal resection of each lobe. The right recurrent laryngeal nerve was visualized. The left nerve was not seen.

Examination of the removed thyroid lobes showed numerous adenomas with scattered areas of hyperplasia. Some of the acini showed small papillary projections.

After operation this patient did well. There was immediate relief from the attacks of coughing and the patient very quickly lost the sensation of cervical constriction and choking which she complained of before operation. Post-operative examination of the larynx revealed normally functioning vocal cords. Since then the patient has done well.

Case 3. A. F., male, aged 41 years, was first seen on October 27, 1933. He stated that for the preceding 2 years, he had experienced frequent attacks consisting of sensation of constriction about the neck, choking, marked "pounding of the heart" and tachycardia, which gave him the feeling of impending dissolution. Immediately preceding these attacks, he noted difficulty in breathing upon inclining his head toward the left side. About 8 months before, he observed an enlargement of the thyroid gland. He consulted a physician who advised immediate hospitalization. Further examination revealed a basal metabolic rate of plus 74 per cent, with hypertension of 280 systolic, and 160 diastolic. In addition, marked cardiac enlargement was noted. After preliminary treatment with Lugol's solution, and other measures, an operation was performed on the thyroid gland at another hospital. The operative notes state that a subtotal removal of the right lobe was done. Patient was confined to the hospital for 2 months after the operation, and then he began to have repeated attacks similar to those he experienced before the operation.

Six months later when I saw him, he presented evidence of a severely toxic Graves' disease with marked psychomotor activity, excessive sweating, nervousness, tachycardia (160), tremor and weakness. He was admitted to the New York Hospital on November 1933. Further examination revealed the scar of the former thyroid operation and moderate enlargement of the left lobe. The trachea could not be clearly outlined. The heart was greatly enlarged, the left border extending to the anterior axillary line. There was systolic murmur at the apex. Blood pressure was, systolic 38, diastolic 90. Pulse, 120, was regular. Basal metabolic rate was plus 43 per cent. Urine examination showed albumin, 4+, few hyaline casts. Hemoglobin was 90 per cent, blood Wassermann was negative. Urea nitrogen was 17 milligrams, blood sugar 93 milligrams, uric acid 4 milligrams per 100 cubic centimeters.

Because of the patient's history of choking sensations, of cervical constriction, of relief in the upright position, and also of relief following turning of the head toward the right, lateral roentgenograms of the neck was made. This showed a forward displacement of the trachea. Another film was made immediately after the swallowing of barium, this indicated forward displacement of the esophagus by a retro-esophageal mass. A pre-operative diagnosis of Graves' disease with a retro-esophageal extension of the goiter was made.

Pre-operative preparation consisted of the administration of Lugol's solution, high caloric intake, sedatives, etc. The basal metabolic rate dropped to plus 13 per cent. Operation was performed on November 1 933. The scar was excised. Considerable scar tissue was found infiltrating the depressor muscles with fixation to the thyroid gland. The gland was finally exposed and was found to present a considerable enlargement of both lobes. In an attempt to dislocate the right lobe after ligation of the superior pole and division of the isthmus, great difficulty was encountered. This was found to be due to a large projection of

Fig 4 Pre-operative lateral roentgenogram of the neck. Case 4, showing the anterior displacement of the trachea which is caused by the presence of a mass in the retro-tracheal region by a retrotracheal mass

Fig 5 Pre-operative lateral roentgenogram of the neck, Case 4, immediately after the ingestion of a barium mixture showing the anterior displacement and angulation of the esophagus by a retro esophageal mass

thyroid tissue extending posteriorly across the midline between the esophagus and the vertebral column (Fig 3) In order to protect the integrity of the recurrent laryngeal nerve, the right lobe was partially resected and bleeding points were ligated A temporary ligature was placed around the inferior thyroid vessels By a process of blunt and sharp dissection, the retro-esophageal projection was delivered into the wound The absence of adhesions in the region, and the ease of delivery of this projection indicated that manipulation at this site had not occurred during the first operation, and that the surgeon had completely overlooked the presence of the retro-esophageal extension A subtotal resection was performed on both lobes, and the wound was closed

Pathological examination of the specimen revealed scattered areas of hyperplasia with papillary projections of the acinar epithelium. The patient did extremely well after operation Laryngeal examination was negative The basal metabolic rate dropped to minus 5 per cent. The patient was discharged on the twelfth day after operation in excellent condition Since then there has been no return of the attacks which occurred so frequently before, and the patient has remained well

I am indebted to Dr Richard Lewisohn for permission to report this case This patient was on his service at the Mt. Sinai Hospital recently and was operated upon by him He recognized clinically the probability of a retro-esophageal goiter and demonstrated the condition by lateral roentgenograms of the neck as already indicated The clinical diagnosis was confirmed at operation

CASE 4. S F, married housewife of 42 years, was admitted to the surgical service of Dr Lewisohn on February 27, 1935, complaining of the presence of a goiter of 7 years' duration, and hoarseness and dysphagia of 9 months' duration During the past 7 years, she had noted a gradually increasing swelling in her neck, confined mainly to the left side. Aside from the presence of the swelling, she had no other symptoms until 9 months before admission when she suddenly noted hoarseness This persisted with varying intensity up to the date of her admission During this same period, she noted frequent attacks of choking brought on especially after inclining her head toward the left side Rotating her head again toward the right side relieved the choking sensation In addition, she noted intermittent difficulty in swallowing

Examination showed an obese female with facial hirsutism, no exophthalmos. There was a large adenoma occupying the right side of the neck and the isthmus, and a smaller, freely movable, cystic adenoma, in the left lobe of the thyroid It was possible to palpate the trachea which seemed to be displaced forward by a posterior mass It was possible to palpate an adenoma which seemed to be attached to the right lobe and pass behind the trachea, and could be moved slightly from side to side Laryngeal examination revealed a right recurrent nerve paralysis The right vocal cord was in the midline There was a small amount of outward motion in the right arytenoid but the cord itself was immobile. The left vocal cord moved normally Blood pressure was 105 systolic, 70 diastolic. Blood count was negative. Hemoglobin was 90 per cent The urine was negative. Blood sugar was 95 milligrams Blood Wassermann was negative Basal metabolic rate was plus 7 per cent. X-ray examination of the chest showed a moderate degree of diffuse dilatation of the aorta. There was no evidence of intrathoracic goiter A lateral X-ray of the neck disclosed the trachea pushed forward by a retro-tracheal mass (Fig 4) Lateral X-ray of the cervical esophagus following the ingestion of barium, showed some constriction of the esophagus and displacement of this organ anteriorly by a retro-esophageal mass (Fig 5) A diagnosis of multiple non-toxic adenomas of the thyroid with retro-esophageal extension was made.

Fig 6 Lateral roentgenogram, of same patient taken 6 days after operation From this picture it is seen that the trachea has returned to practically normal position

Fig 7 Lateral roentgenogram of same patient 6 days after operation, following the ingestion of barium mixture showing the return of the esophagus to normal position and the correction of the anterior angulation

Operation was performed by Dr Lewisohn on March 4, 1935 There was large adenoma occupying the right lobe Some difficulty was encountered in completely dislocating the right lobe due to the presence of a large adenoma measuring approximately 3½ by 1½ inches, extending from the right side behind the esophagus almost across the midline It was possible to roll this adenoma out of its retro-esophageal position, and to perform partial resection of the right lobe The left lobe contained a large adenoma which also was removed

Convalescence was quite uneventful. There was almost immediate relief of practically all her symptoms with the exception of hoarseness. At the time of her discharge from the hospital on the tenth day after operation, laryngeal examination showed the right vocal cord to be immobile The operative wound had healed by primary union

CONCLUSIONS

1 Retro-esophageal goiter is a definite clinical entity which may be diagnosed before operation

2 Characteristic symptoms are sense of constriction about the neck attacks of choking especially when turning the head away from the side of entrance of the goiter in the retro-esophageal space spells of coughing dysphagia and hoarseness of variable intensity

3 The probable diagnosis of a retro-esophageal goiter should be kept in mind if it is possible to determine anterior displacement of the trachea against the upper edge of the manubrium

4 Retro-esophageal extension of a goiter may be graphically depicted by lateral roentgenograms of the neck showing anterior displacement of the trachea and also after the ingestion of a barium mixture to outline the position and shape of the esophagus

5 The operative technique is discussed

HYPERTROPHIC CRICOPHARYNGEAL STENOSIS[1]

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IN the recent literature, attention has been directed to benign disorders of the upper esophagus resulting in dysphagia and malnutrition This type of dysphagia is usually the result of unstable emotional states, malnutrition, and anemia, especially that form of anemia associated with glossitis, vitamin deficiency, achlorhydria, and splenomegaly It is generally believed that the upper and lower ends of the esophagus are normally in a state of tonic closure and that the usual cause of benign spastic dysphagia is some neuromuscular dysfunction At the entrance of the esophagus the comparatively powerful cricopharyngeus muscle is responsible for its tonic closure Branches of the glossopharyngeal (ninth cranial nerve) and the vagus (tenth cranial nerve), together with some fibers of the cervical sympathetic system, form the pharyngeal plexus, which in turn innervates the constrictors of the pharynx as well as the pharyngeal mucosa Therefore, the cricopharyngeal muscle is subject to both sensory and psychical stimuli Any series of sensory stimuli, if continued to a point of causing irritation of the mucous membrane, would therefore set up a vicious cycle, as would also psychical stimuli resulting from severe emotional reactions

Hypertonicity, spasm, or inefficient relaxation (achalasia) may lead to passive congestion, edema, round cell infiltration, hypertrophy, and degeneration of muscle fibers, and finally, fibrosis It is significant, however, that long standing so called cardiospasm of the lower esophagus does not lead to muscular hypertrophy of the cardiac portion of the esophagus

We have had the opportunity of examining and operating upon a patient who presented a benign tumor of the cricopharyngeus muscle due to hypertrophy and degeneration of its fibers, together with intracellular edema, probably as a result of a long standing neuromuscular dysfunction Our pre-operative diagnosis was incorrect in that we expected to find a parathyroid tumor or an atypical thyroid tumor encircling the esophagus With the tumor exposed, we believed it to be an inoperable neoplasm and, thinking to afford the patient a certain degree of palliation, carried out what we believe is a new operative procedure The patient is now alive, well, and symptom free, 20 months after operation Preoperative data and postoperative follow-up are complete, and as material was obtained for microscopic study, we believe that it is justifiable to report this case in some detail, hoping that our

Fig 1

Fig 2

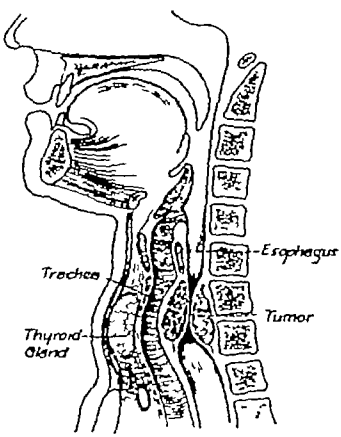

Fig 3

Fig 1 Pre-operative lateral view of the neck showing the smooth mound-like swelling in the midline It was at first thought to be of thyroid gland origin.

Fig 2 Roentgenogram showing the smooth funnel shaped narrowing of the esophagus opposite the level of the fifth and sixth cervical vertebræ

Fig 3 Diagrammatic sagittal section showing the esophageal obstruction, tracheal compression, and thyroid prominence which were brought about by the post-cricoid tumor

From the Surgical Service of the Fifth Avenue Hospital Dr F W Bancroft Director

Fig. 4. Diagrammatic cross section of the neck at the level of the esophageal lesion showing its relation to the surrounding structures and adhesions to the thyroid gland and trachea.

observations may be of some help to the surgeon unexpectedly confronted with a similar situation.

The patient, an American housewife, 40 years of age, was first seen at the request of her family physician, February 27, 1933, because a piece of meat had lodged in her upper esophagus necessitating removal by means of a forceps. She gave a history of having noted a "thyroid enlargement" of 6 years' duration, associated with rare attacks of palpitation. She was otherwise well, until 1 year before admission when she noted intermittent dysphagia and a feeling that food stuck at the lower neck level. Six months later she became definitely unable to swallow meat and it was eliminated from her diet. There

Fig. 6. Photomacrograph of the biopsy material removed at operation. It shows edema and fibrosis together with hypertrophy and degeneration of striated muscle fibers.

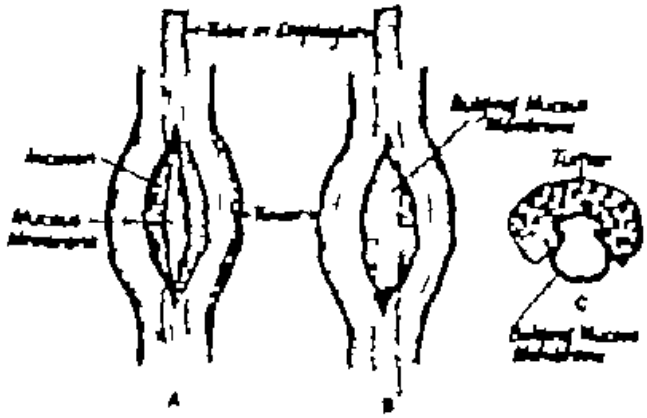

Fig. 5. Operative steps. A, A tube has been placed in the esophagus and a longitudinal incision made through the tumor down to the esophageal mucous membrane. B. The mucous membrane is shown bulging through the incision. C, A cross section showing how the lumen of the esophagus was enlarged by the incision of the tumor down to the mucous membrane.

had been only slight loss of weight, although the diet was limited to liquids and soft solid foods. She had been nervous and irritable for 3 years and admitted having had bad temper.

Examination of the neck revealed a smooth, rounded, mound like swelling in the midline at the level of the thyroid gland isthmus (Fig.). It was diffuse, fairly soft, attached to the underlying trachea, it moved when the patient swallowed and measured 4 5 centimeters in its transverse and longest dimension. There was no cervical lymphadenopathy. Intraoral and laryngeal examinations revealed no abnormality.

Laboratory findings showed: ( ) Basal metabolism rates on occasions were —1 and +6. ( ) X ray films taken after the ingestion of barium meal showed a smooth area of esophageal constriction at the level of the fifth cervical vertebra (Fig. 3). (3) A separation biopsy was attempted but the nature of the cells could not be determined. (4) Esophagoscopy was carried out after cocainization of the pharynx with 10 per cent cocaine, and a 9 millimeter esophagoscope was passed readily to the level of the cricopharyngeal constriction, where the instrument met an obstruction due to spasm or extrinsic pressure. The lumen was narrowed considerably and the mucous membrane presented 3 longitudinal folds and appeared somewhat puckered. Under direct vision a 7 millimeter olive tipped bougie could, with difficulty be forced through. A definite esophagoscopic diagnosis was made but it was felt that the esophageal condition was due to extrinsic pressure. (5) Blood count and urinalysis were normal. (6) Further fluoroscopic studies during the ingestion of barium paste showed a narrowing of the lumen of the esophagus at the level of the sixth cervical vertebra, where the barium was seen to pass slightly to the left of the midline. In the lateral direction the narrowing was the same as seen in the anteroposterior direction, and the involvement was over an area of approximately 3/4 inch. The trachea showed evidence of posterior pressure. Dr. R. E. Pound, who made the radiographic studies, suggested that the esophageal condition might be secondary to pressure from an enlarged thyroid which had extended around the trachea posteriorly and pressed on the esophagus.

An exploratory operation was decided upon and carried out under intratracheal anesthesia, March 24, 1933. The usual collar incision for a thyroidectomy was done and

A B

Fig 7 A and B, Postoperative roentgenograms after ingestion of barium, showing the increased width of the esophageal lumen and its lateral position

both lobes of the thyroid were mobilized After considerable careful dissection, it was decided that the tumor was inoperable and it was incised longitudinally along its left lateral border down to its mucous membrane which then bulged through the incision On cut section, it was about 1 centimeter in thickness and it looked and felt like cartilage A piece of this tissue was removed for biopsy purposes and a frozen section was done A Levine tube was passed through the esophagus into the stomach Both lobes of the thyroid were then replaced and a wick of gauze was inserted on each side and a routine closure was done without incident (Figs 3, 4, 5)

The material removed at operation for microscopic examination was described by Dr C Zent Garber as follows "Macroscopical examination of the specimen removed at operation measured 7 by 3 by 3 millimeters It was of a yellowish pink color, smooth surfaced, and quite firm Microscopical examination showed a border of dense fibrous tissue surrounding some small blood vessels Adjacent to this there was much striated muscle The fibers stained a dull pink, the cytoplasm was granular, the cell outline poorly marked and the nuclei stained poorly No tumor cells or inflammatory cell reactions were seen Further sections showed some degeneration of muscle fibers and some fibrous and adipose tissue."

The postoperative course was stormy and complicated by acute embolic nephritis, right otitis media, right mastoiditis, and an operative paralysis of the left recurrent laryngeal nerve Her convalescence was slow but she was discharged from the hospital much improved 37 days after the operation

Postoperative X-ray films after the ingestion of barium paste, have been taken periodically and show (Figs 7a and b), that the esophageal lumen is somewhat enlarged and is located to the left of its pre-operative midline position On fluoroscopy the barium is seen to pass through this area without delay

The patient has made steady progress and is now robust and healthy The neck mass has largely disappeared (Fig 8) Her voice is somewhat less husky, although the left side of the larynx is still partially paralyzed She eats a full diet without any difficulty

Fig 8 Postoperative photographs of neck.

SUMMARY

Our findings, operative procedure, and results, bear a striking similarity to the condition which Rammstedt first described in reporting his operation for congenital hypertrophic pyloric stenosis

Bougienage in this case was attempted but the pathological condition found at operation showed clearly why adequate stretching of this area would not have been possible

The procedure described has not been reported previously as far as we have been able to learn from a review of the available literature

NOTE —Dr James B. Woods of Tsinghkiangpu General Hospital, China, in a personal communication, states that he has seen a number of his Chinese patients who after a prolonged fit of temper absolutely uncontrolled, show definite symptoms of stricture of the esophagus In a number of cases this symptom persists and if untreated some of these patients die of dehydration and starvation hole others pass over into a chronic type of esophageal stricture where fibrosis has taken place to greater or lesser degree. For want of a better name the condition is known in China as anger disease."

COMBINED ONE STAGE CLOSED METHOD FOR THE TREATMENT OF PHARYNGEAL DIVERTICULA[1]

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WITHOUT using too many cumbersome definitions and boring classifications, the writer nevertheless, deems it necessary to arrange pharyngeal diverticula in definite groups based on the literature to which he has had access and on his personal operative experience in 79 cases. Clarity of definition usually promotes the advancement of any subject. The time has come for more accurate classification of the so called "pulsion esophageal diverticula," which really arise in the pharynx and should therefore be named, accordingly "pharyngeal diverticula." There are no recorded cases of true pulsion diverticula of the esophagus. The cases recorded as diverticula of the esophagus arise either opposite the bifurcation of the trachea or at the lower end of the esophagus. They are not pulsion in origin but result from peri-esophageal inflammation and are, therefore traction diverticula. They are mentioned here to emphasize their difference in etiology from the pulsion pharyngeal diverticula.

HISTORY OF PHARYNGEAL DIVERTICULA

These diverticula are usually incorrectly termed in the literature esophageal" (Killian Jamison and Moynihan) There is no doubt that credit for the first observation of pharyngeal diverticula belongs to Mr Ludlow He furnished illustrations and an accurate description of this then unknown condition to Dr William Hunter in the year of 1764 Later descriptions were made by Monroe in 1811, and by Sir Charles Bell in 1816. The name of Matthew Baillie is also associated with an early description of this condition.

About 1850 Kluge had the idea of extirpating the sac. Nichans in 1884 was the first to extirpate the sac.

The common method of treatment had been by bougies. As early as 1848, Dendy attempted to obliterate diverticula by means of caustics. In 1871 electricity in the form of faradization was used by Waldenberg. It is now obvious that since the year of 1848 these pharyngeal pouches were not as common as we have been led to believe. Furthermore it would seem that some of these ancient plans of conservative treatment have survived even to the present day

The postmortem examination of Whitehead's patient reported in 1891 showed that the pharyngeal pouch consisted of all three coats of the pharynx, and was observed at the junction of the pharynx and the esophagus. This is contrary to the belief that all of these pouches arise as herniations of the mucous membrane While it is difficult to believe that a hernial sac can contain all of the musculature which makes up the parent structure the writer has had a similar case In the reporter's case the wall of the sac consisted of all of the coats of the pharynx. The pouch, however did not arise from the junction of the esophagus and the pharynx, but at a much higher level from the lateral wall of the pharynx

While S J Mixter, in 1894, had cut into one of these pouches and had removed enough of the sac to make the esophagus a straight tube from the "spur" up, his operation was apparently not one of deliberate extirpation of the sac. After reading both reports carefully the writer believes that the operation performed by W Joseph Hearn in 1896 and reported in 1899 was the first deliberate extirpation of the sac in the United States. Hearn's operation was performed in the Jefferson Hospital.

Girard, of Berne in 1896 deeply impressed by the mortality of the operations that had preceded his two cases, devised a technique with which to invaginate the sac without opening into the esophagus. This method of treating the sac has

[1] The preliminary report of this paper was read before the Philadelphia County Medical Society on March 1912 DeCosta Night (in honor of Dr John Chalmers DeCosta)

been used by Albert Edward Halstead, J B Murphy, A D Bevan, and others

Henry T Butlin's contribution in 1898 added very little to that already promulgated by his predecessors His technique did not differ from Barrow's technique except that he used silk sutures instead of catgut

In 1900, Richardson reported a plastic operation on the esophagus below the pharyngeal pouch The writer can find no other recorded cases in which this procedure was found necessary

A distinct contribution to this subject was by A Bois Barrow in 1905 Barrow used a bougie in the pouch during the course of the operation This does not differ in principle from our present plan of treatment except that we now use the esophagoscope instead of the bougie in order to facilitate identification of the pouch Barrow's method of treating the neck of the pouch does not differ from our present plan He reflected back the muscle at the neck of the sac and ligated the mucous membrane inside of the reflected cuff, then, by stitching over the muscles of the hypopharynx, he buried the ligated mucous membrane

Since these early cases, many operations for the cure of pharyngeal diverticula have been advocated These operations may be classified as the one and two stage operations Here, nothing but extirpation of the pouch is considered because the writer has performed no other operation for the cure of pharyngeal diverticulum

It is the belief of the reporter that all operations of extirpation of the sac were one stage procedures until 1910 when C H Mayo performed and advocated extirpation in two stages in order to avoid the possibility of a neck infection descending into the mediastinum The technique of the two stage operation was developed by E S Judd and C H Mayo until the latter, in 1923, could report 74 two stage operations with but 3 deaths The two stage operation has been adopted by Charles Gordon Heyd, Frank H Lahey, Eugene H Pool, and by many others

Lupke, in 1921, reported that he had operated upon 39 cases by the one stage method of extirpation of the sac There were 2 deaths 1 from mediastinitis, 1 from hemorrhage

In the last analysis, the surgeon must be guided by his own experience Thus far the writer has had no reason to abandon the one stage operation Bensaude, Grégoire and Guénaux, in 1922, in discussing the statistics compiled by DeWitt Stetten, note that the mortality between 1900 and 1909 is lower than between 1886 and 1900 These three authors think that the fear of infection of the cellular tissues of the neck and of the mediastinum are without much foundation These authors have collected 109 cases with one stage operations In this series, there were 12 deaths of which 3 were caused by septic cellulitis of the neck. In 23 cases, there had been more or less prolonged suppuration of the peri-esophageal cellular tissue These complications became rarer as operative technique improved (Bensaude, Grégoire and Guénaux)

Moynihan, in his scholarly analysis of this subject in 1927, has insisted that these pouches are from the pharynx and should be called "pharyngeal"

THE SITE OF ORIGIN OF PHARYNGEAL DIVERTICULA

For many years it had been almost universally accepted that pharyngeal diverticula arose from Laimer's triangle This belief persisted until 1908, when Killian wrote his epoch making article on the anatomy of the esophagus and pharynx Killian, not being satisfied with the previous dissections done by Luschka and later on by Laimer, resolved to study the region of the hypopharynx and the esophageal orifice

Much of Killian's labor had gone for naught until Sir Berkeley Moynihan investigated the subject in 1927 In his article, Moynihan corrected the erroneous belief that pharyngeal diverticula arose from Laimer's triangular area He pointed out that Laimer's triangular area is situated below the lower border of the cricopharyngeus muscle of the pharynx. He emphasized the fact that diverticula did not arise in Laimer's triangular area by stating that there were no recorded cases originating in this area

Killian further demonstrated another possible area for the origin of the pharyngeal diverticula He showed the presence of a defect below the cricopharyngeus muscle He called this defect a slit. This slit is below the cricopharyngeus muscle and above the esophageal fibers Killian's description is as follows "The slit that we see on each side between the pars fundi-formis and the circular fibers of the esophagus is a very important area. Here in this slit the recurrent nerve passes through to divide into the anterior and posterior branches" Killian makes no mention of this area in its relationship to diverticula of the pharynx It is quoted here because of the work recently reported by Moynihan on dissections made by J K Jamison It is because of this original work, done by Killian and confirmed by Moynihan, that we are attempting to establish in this series of cases the relative frequency of this site for the origin of pharyngeal diverticula

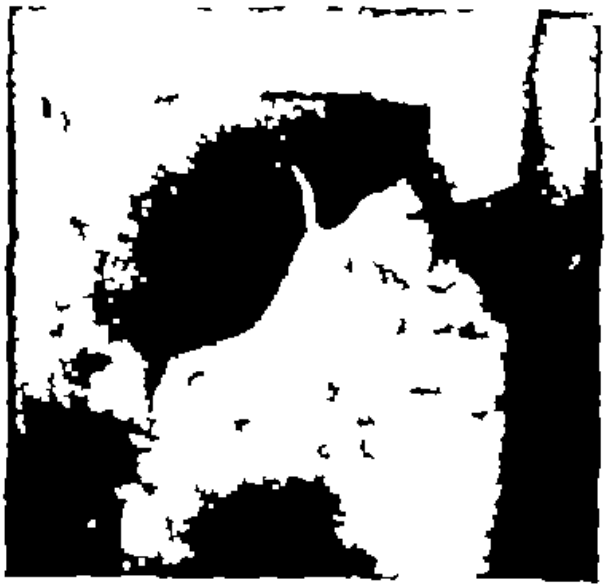

Fig 1 Double diverticulum as shown by X-ray plate

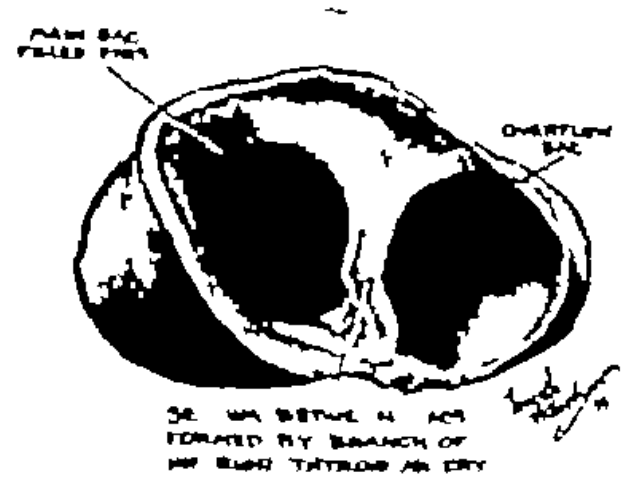

Fig Gross specimen of pharyngeal diverticulum which has bifurcated by a branch of the inferior thyroid artery

Killian's studies demonstrated that the lowermost bundle of the inferior constrictor muscle, which he calls the sling bundle of the pars fundi formis, is the chief closing muscle of the esophageal opening In the state of contraction it presses the opening of the esophagus together and holds it against the cricoid plate, thereby producing a *crescent shape with the concavity forward.* In his text and by photograph, he further points out the influence of the cricopharyngeus muscle in the production of pharyngeal diverticula.

The observation of Jamison, while not original, certainly has crystallized our knowledge of the subject. He observed not only the inferior branch of the recurrent laryngeal nerve, but also a branch of the inferior thyroid artery and vein and a bundle of lymphatics passing through this hiatus. This anatomical observation of Killian and Jamison explains the symptom of hoarseness which was present in 9 of our patients Likewise, it *explains the presence of hoarseness which temporarily followed* 2 of our operations. A curious fact concerning the postoperative hoarseness was that it was not apparent immediately after operation but came on gradually after the fifth day The hoarseness in both cases, fortunately entirely disappeared.

That this slit is not an uncommon site for the origin of a diverticulum is further emphasized by the frequent presence of a branch of the inferior thyroid artery crossing the fundus of the sac. We have had occasion to ligate this vessel in at least 35 per cent of our cases. We believe that the deformity of the fundus of the sac, as shown by X-ray pictures (see Fig 1) is caused by the entrance of a branch of the inferior thyroid artery into this slit. If this be so, this supposedly unusual site of origin for diverticula would prove to be a common one for the origin of pharyngeal diverticula.

The presence of a double diverticula (see Fig 2) could be explained by the presence of a larger branch of the inferior thyroid artery which was *too resistant to yield with the sac and* consequently bifurcated the opening at the neck of the sac. Indeed it is our belief that a diverticulum can arise from any portion of the pharynx which is perforated by a branch of the inferior thyroid artery (see Fig 3) This belief is fortified by the origin of a diverticulum much higher than the cricopharyngeus. The defect of the oblique fibers in the posterior lateral wall of the inferior constrictor muscle appeared as though it had been punched out with an instrument. The sac was covered with a thick muscular coat—the only diverticulum in this collection which had a muscular covering The X ray and bronchoscopic studies confirmed this high origin of the sac. Dr Manges reported, "a rather large diverticulum originating a little higher than the average apparently just below the larynx." Because of the unusual covering and high origin, I performed a two stage operation. The second stage consisted not only of the removal of the sac but also of the repair of the pharyngeal defect

Briefly true pulsion diverticula have been observed by us to originate in one of three areas. (1) They have arisen most frequently in our experience, from the commonly described area above the cricopharyngeus muscle, either on the left or on the right side more frequently on the left In 4 of our patients the pouch originated

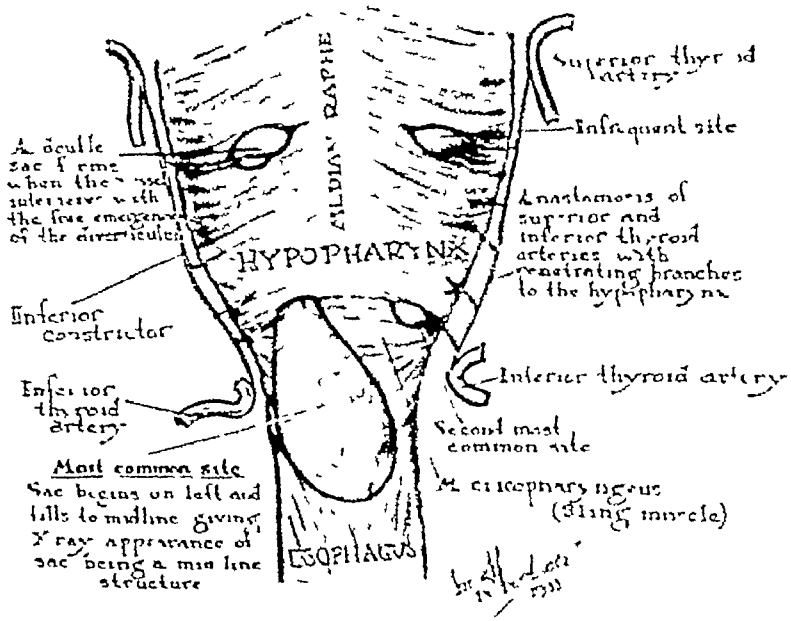

Fig 3 The pharynx, posterior view showing the various locations for the development of diverticula

from the right side of the pharynx (2) The next place in the order of frequency for the origin of the diverticula in this series, was the Killian-Jamison area This is on the posterolateral wall of the pharynx, below the cricopharyngeus and above the circular muscle fibers of the esophagus Through this weak area the inferior laryngeal nerve, a branch of the inferior thyroid artery and a bundle of lymphatics pass In this area more than 35 per cent of the pouches arose (3) The location least frequent for the origin of the diverticula has been through the lower portion of the inferior constrictor muscle, a site for another branch of the inferior thyroid artery

PHYSIOLOGY

It would seem that some other factor or factors, aside from the neuromuscular co-ordination of the pharynx and the esophagus, must be considered in a careful analysis of the physiology of swallowing The act of deglutition differs for liquids and for solids The phenomena observed in swallowing liquids is manifested by a rapid rise of pressure within the pharynx, which is almost instantly followed by a projection of the liquids with great force into the esophagus Second, in the course of swallowing solid food, there is a temporary arrest of the bolus of food in the pharynx The further passage of solid food depends upon the action of the constrictors of the pharynx Analyzing these two accepted physiological facts, it would seem that a ready explanation for the beginning of herniation in the pharynx is found in the muscular weakness at one of the vulnerable points already described Once begun in this manner, the further progress of the herniation is stimulated by each act of swallowing of liquid

By experiment it has been demonstrated that at the beginning of deglutition there is a sudden rise of pressure, the result of a quickly acting force resident in the mouth or pharynx, in consequence of which the liquid foods are rapidly shot down toward the end of the esophagus, peristalsis playing no part in the process The proof of these statements was furnished by Meltzer It was found as a result of many experiments by the aid of esophageal and pharyngeal balloons connected with tambours, that the pharyngeal and esophageal pressure was simultaneous when liquids were swallowed From this it was inferred that liquids were projected or shot down The pharyngeal and esophageal balloons are both compressed at the same instant.

These facts demonstrate that deglutition consists of two phases

Fig 4 Malignant diverticulum. Showing the existence of carcinoma in pharyngeal diverticulum A distant pouch with irregularities in its base

1 A rapid rise of pressure in the pharynx, as a result of which, liquid or semi-liquid foods are suddenly shot down to the lower end of the esophagus.

2 A peristaltic contraction of the musculature of the canal, which, acting as a supplementary force, carries onward any particles of food in the canal and forces the bolus through the esophagogastric orifice which is now opened by a relaxation or inhibition of the sphincter cardiac muscle.

The immediate cause of the sudden rise of pressure was shown by Meltzer to be the contraction of the mylohyoid muscles. These muscles are probably assisted in their action by the contraction of the hyoglossus muscles as well as the tongue itself

SYMPTOMS OF DIVERTICULA OF THE PHARYNX

1 Dysphagia is the most common symptom of diverticula of the pharynx. The dysphagia varies from absolute inability to swallow liquids or solids to a relatively small degree of inconvenience in swallowing In the beginning, when the pouch is small, the individual is able to swallow after the pouch is filled but, as the pouch increases in size it frequently assumes a position between the esophagus and the vertebral column, so that, when the pouch is filled, it presses on the lumen of the esophagus to such a degree as to render swallowing utterly impossible

2 Vomiting is a prominent symptom. Regurgitation of food from a partially filled sac is frequently an annoying condition. This varies from immediate regurgitation as soon as the sac is partially filled, to regurgitation a number of hours after eating Indeed stagnated food, regurgitated at night, often produces chronic bronchitis. In fact, one of the first symptoms complained of by the patient is regurgitation of undigested food mixed with saliva.

3 Many patients complain of noisy deglutition. This symptom is commonly so annoying as to cause the patient to eat alone. A number of patients of the writer never ate in the presence of others or in public. One patient waited to eat until the rest of the family had dined

4. Hoarseness is not an uncommon symptom Nine patients in this series complained chiefly of hoarseness.

5. A tumor occasionally in the neck may be palpated. This sign was present in 5 patients of this series. Invariably a gurgling sensation could be detected beneath the fingers, when the patient swallowed.

While the symptoms described, when present, are helpful in leading one to suspect the presence of a diverticulum, the diagnosis is invariably made during X ray or fluoroscopic examination While the report of the roentgenologist's findings may usually be accepted as conclusive, uncertainty arose in 3 cases of this series, because of distortion of the fundus of the sac (see Fig 4) The question was settled conclusively by the esophagoscopist. One patient had a carcinoma in a pharyngeal pouch, another had a pharyngeal diverticulum. Subsequently, resection of the hypopharynx and cervical esophagus showed a carcinoma in the fundus of one sac. This patient lived for 3 years following the operation. The other sac was distorted by adhesions and a branch of the inferior thyroid artery and was not malignant.

PROGNOSIS

The question of mortality in diverticulum of the pharynx has undergone a revision in recent years. Now diverticula of the pharynx are recognized early The sac does not reach the dimensions that were observed in our early series of cases, consequently now the patient's physical condition when operation takes place, is much better than formerly It was not unusual in our early cases to resort to gastrostomy preceding the operation for diverticulum. (For early procedure, see the original paper by Chevalier Jackson and the author) We have not done a preliminary gastrostomy on the last 50 patients

THE MORTALITY OF VARIOUS TYPES OF OPERATION

Much is said, by those who advocate the two stage operation, of the high mortality due to mediastinitis which follows the one stage operation Where this opinion had its origin, we do not know, nor have we been able to find any record of the high death rate due to mediastinitis in recent years Certainly, it has not been a complication in any of our 76 cases We believe that mediastinitis should not occur any more frequently in the one stage operation than in the two stage operation The easy access to the sac, its rapid separation from the lateral and posterior wall of the esophagus, is only possible when an esophagoscope is in the sac The esophagoscope is of invaluable aid until the neck of the sac is reached, then it is temporarily withdrawn

Secondary hemorrhage is often quoted as a complication of the one stage operation This is without foundation in our experience We have not had any secondary hemorrhages in any of our pharyngeal diverticula In 1926, a death occurred due to secondary hemorrhage This mortality was not in a case of pharyngeal pulsion diverticulum but it occurred in a patient suffering with a traction diverticulum In this case, part of the pharyngeal wall was purposely resected This patient is not reported in this series, as it is not a case of pulsion diverticulum

Recurrence of the sac occurred in 2 patients of this series In 1 patient, 67 years of age, there was a double diverticulum which involved practically all of the lower lateral pharyngeal wall We believe that this recurrence could have been avoided if a longer interval than 6 months had elapsed between the removal of the first and second pouch The second recurrence was in a patient in his late sixties with a very poorly developed musculature of the pharynx This diverticulum arose from the Killian-Jamison area Both patients have been re-operated upon by me, and there has been no recurrence in 10 years in the first and 3 years in the second case

Pulmonary complications not infrequently follow the operation Many of these patients have a pre-operative bronchitis as a result of overflowing of the contents of the pouch into the larynx There is a spilling of the foul contents of the sac, usually during sleep, and this infected liquid flows through the larynx into the bronchi, so that clinically, bronchitis is often an associated condition One of our two fatalities in pharyngeal diverticula was due to a diffuse pneumonia

Renal complication was responsible for the other death, the patient, 67 years of age, dying of uremia 48 hours after operation

Fig 5 Atresia of the esophagus The barium had been introduced into the lower end of the esophagus through a gastrostomy

Temporary pharyngeal fistula occurred in 5 of the early cases This has been obviated in subsequent cases by an improvement in our technique

Wound infection as a complication has been noted to occur in those patients in whom the omohyoid muscle had been sutured We now divide the omohyoid muscle only when such division is necessary in order to prevent trauma to the sac during its delivery When it is necessary to divide the omohyoid muscle, it is not sutured

We have now considered all the immediate and remote complications associated with our one stage operation

We believe that the 2 deaths reported in this series might have been avoided if intratracheal ether anesthesia had not been used We have discontinued its use and have substituted ether anesthesia by rectum The last case was done under avertin anesthesia

We are not in accord with those who believe that the two stage operation for diverticula indicates recent surgical progress, because the two stage operation is supposed to eliminate mediastinitis as a postoperative complication Mediastinitis has not been a complication in any of the 76 one stage operations performed by us

The writer admits that the two stage operation, as it is done today, far surpasses the older methods of treatment, by eliminating most of the dangers of the one stage operation as it was done in the past The two stage operation is not logical, because, inasmuch as the diverticulum is a hernia of the pharynx, no effort is made in the two stage operation to repair the pharyngeal defect This operation simply removes, in the first stage, the redundant sac, and, in the second procedure, the secreting mucous membrane of the remaining portion of the sac The very basis of the cure depends upon traction on the pharynx which frequently distorts this structure as well as the upper portion of the esophagus, obliteration of the pha-

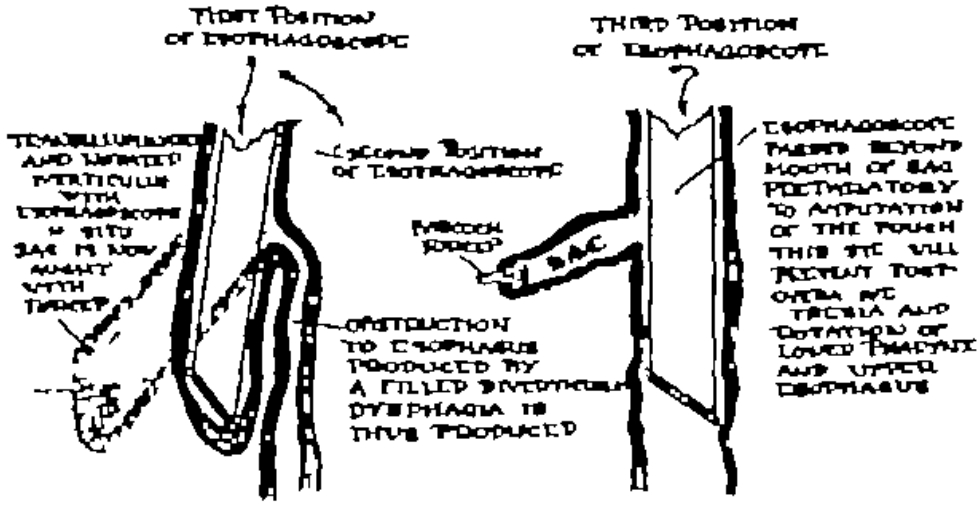

Fig 6 Diagram showing internal manipulation by the esophagoscopist

ryngeal opening at the neck of the sac by scar tissue rather than by surgical repair as is done in the one stage operation.

One writer cautions those who contemplate doing the two stage procedure of the strong probability of entering the sac during the dissection necessary for the separation of the sac from the esophagus, again he warns the operator of the probability of entering the sac while freeing it at the neck again he cautions the operator not to enter the sac while suturing it to the muscles in the incision. If he accomplished the delivery of the sac and its fixation without perforation, other complications may be anticipated Angulation of the pharynx may cause complete atresia Necrosis of the sac may follow distention. The necessity of postoperative passage of bougies *may ensue for at least a year With these complications* as possibilities and occasional occurrences following the work of one of the great surgeons in this country any operation for diverticulum of the pharynx should be considered a serious one.

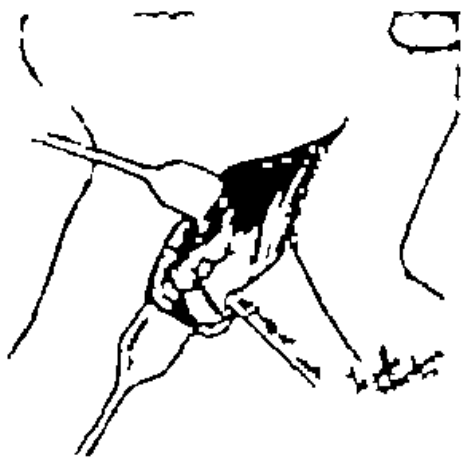

Fig 7 Showing the incision in the neck and the retracted thyroid gland The esophagoscope is in the pouch illuminating the fundus An aberrant vessel is shown crossing the fundus of the sac

There is no doubt that the two stage operation is the operation of choice when the surgeon either discards the aid of the esophagoscope or when the aid of the esophagoscope is not available This fact is strongly emphasized by the pathetic condition of two patients who were operated on by the one stage operation, without the aid of the esophagoscope Both of these patients were operated upon outside of Philadelphia. These patients were admitted to the Bronchoscopic Clinic, both had atresia of the esophagus One had paralysis of the recurrent laryngeal nerve. In one of the patients, a portion of the *esophageal wall had been excised and the pharyngeal* pouch was not touched (Fig 5) The X ray picture shows absolute block of the esophagus. The barium had been introduced into the lower end of the esophagus through a gastrostomy fistula The writer did a reconstructive operation on the esophagus of each of these patients, with the aid of the esophagoscope which was introduced through the mouth and the gastrostomy fistula Dr Louis H. Clerf assisted in these procedures Both patients are now swallowing satisfactorily

We believe that the operation of choice is the one which at its completion leaves the pharynx and the esophagus in their normal positions not angulated not stenosed This operation should not only remove the redundant sac but repair the defect in the pharyngeal wall *In the ideal* operation, danger of rupturing the sac, either in freeing it from its bed or separating it at the neck, is reduced to a minimum by the aid of the

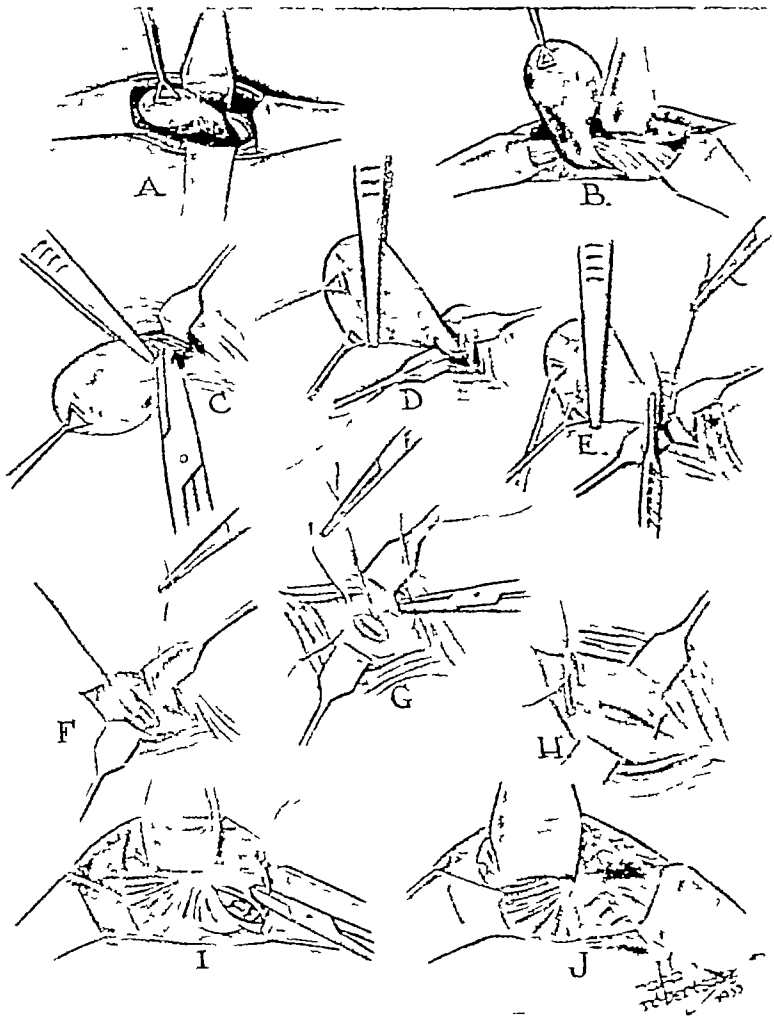

Fig 8 The various steps in the operative procedure

esophagoscope (Fig 6) The operation to be selected is the one which eliminates the risk of penetrating the sac during its fixation to the muscles in the incision We believe that all of these desiderata are combined in the one stage closed operation with the aid of the esophagoscope

This procedure was first advocated by Jackson, and he, in conjunction with Gaub, reported 2 cases in 1915 Since then, the writer has entirely modified the surgical technique The operative procedure which has been described herein is not Gaub's technique, but one which was devised by the writer

TECHNIQUE AT OPERATION

Under rectal ether anesthesia, intratracheal or avertin, the patient is prepared in the usual manner and an incision is made on the side on which the sac presents and along the anterior border of the sternomastoid muscle (Fig 7) The incision is to reach from the level of the hyoid bone to 1 inch above the sternum and is to pass through the skin, platysma and deep fascia, exposing the anterior belly of the omohyoid muscle This muscle may be divided transversely, or retracted With this incision the external jugular vein may be exposed, and if it is, it should be divided and tied The common carotid artery and the internal

jugular vein are *now exposed and retracted outward*. If the thyroid gland is decidedly enlarged, it is sometimes necessary to ligate and cut the superior thyroid artery. *The trachea and the* esophagus will be found to be encased in a common sheath, which is to be incised, exposing the esophagus in the *posterior part of the wound and* the trachea anteriorly. After this incision has been made the trachea and thyroid are then retracted *toward the midline*.

The esophagoscope is introduced by the esophagoscopist. The sac is emptied by aspiration thereby avoiding expressing the contents into the larynx. The interior of the pouch and the lower pharynx are then painted with an antiseptic solution. The esophagoscope is then introduced into the fundus of the diverticulum and the sac transilluminated then the esophagoscopist rotates the sac into the wound (Fig. 8, A). The sac is grasped with intestinal forceps and drawn upward and outward (Fig. 8, B). The esophagoscope is then withdrawn from the pouch. The sac is then freed to the junction of the diverticulum with the pharynx (Fig. 8, C). Care must be exercised to free all muscle fiber from its neck. The neck of even the largest diverticulum is seldom one-half inch in diameter. A neck larger than this usually means incomplete dissection. The sac is then transfixed at its junction with the pharynx with a small intestinal needle carrying No. 1 chromicized catgut in much the same manner as a hernial sac is transfixed (Fig. 8, D). The neck of the sac is severed close to the pharynx (Fig. 8, E). The stump is cauterized with pure phenol (Fig. 8, F). After transfixation, ligation, and amputation, the stump is invaginated with two mattress sutures of No. 1 chromicized catgut, one above and one below the stump (Fig. 8, G and H). These sutures penetrate only the submucous coat of the pharynx. This invaginated area is then covered by suturing together the cricopharyngeus and the inferior constrictor muscle. If the pouch originates at Killian's slit, the cricopharyngeus and the upper circular fibers of the esophagus are united (Fig. 8, I and J). Here care must be exercised, not to include the inferior laryngeal nerve. During this procedure of muscle repair the esophagoscope is in the esophagus. This detail is absolutely necessary in order to obviate stricture at the esophagopharyngeal junction. If this precaution be followed, none of the patients will require subsequent dilatation of the esophagus.

The incision in the neck is closed in layers, no drainage being used except a *small piece of rubber tissue* or cell-silk placed beneath the deep fascia.

RÉSUMÉ OF STATISTICS

Age	
Youngest	40 years
Oldest	75 years
Average	59 years
Sex	
Male	84%
Female	16%
Length of present illness	3 months to 40 years
Preliminary gastrostomy	3
Average time between operation and discharge	3 days
Type of operation	
1 stage	76
2 stage	3
Complications	
Acute dilatation of heart	2—(recovery)
Uremia	1—(death)
Pneumonia and atelectasis	1—(death)
Anesthesia	
Intratracheal	
Rectal	
Avertin	
Esophagoscopist	
Dr Chevalier Jackson	
Dr Louis H Clerf	67

SUMMARY

1 In a series of 76 pharyngeal diverticula, all operated on by the one stage method, there were 2 deaths.

2 Seventy-four patients had complete recovery

3 None of the cases was complicated by mediastinitis

4 None of the cases required postoperative esophageal dilatation

5 The use of the esophagoscope prevents angulation, stenosis, and atresia of the esophagus.

6 Hoarseness is often a chief complaint

7 There are 3 areas of the pharynx from which diverticula may arise

8 The one stage method of operation is the reasonable method of treatment of pulsion diverticula of the pharynx.

9 The results depend upon rational surgical procedure and accurate approximation of tissues

ADDITIONAL NOTES

Moynihan (Surg, Gynec & Obst Vol 54, 1932) believes that there is no need for operations in two stages He has operated upon 15 cases and *has 'never had any difficulty in obtaining* healing by first intention

Torek (Ann Surg Vol 97 1933) says "Thirty years ago the mortality was very high with the one stage procedure but in the last 5 years, 60 cases have been recorded with a mortality of only 1

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DIVERTICULA IN THE ANTERIOR URETHRA IN MALE CHILDREN[1]

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DIVERTICULA of the urethra may occur in both males and females. In males the diverticulum may be located in the anterior or in the posterior urethra and it may be congenital or acquired. In general, it may be said that urethral diverticula are rare and in children especially rare. A brief survey of the literature reveals only 20 cases in which the diverticulum was located in the anterior urethra in male children.

Because the condition is so rarely found I wish to report the following case.

J. C., male, aged 6 months, was admitted to the Children's Memorial Hospital on February 18, 1934, on the service of Dr. C. A. Aldrich, to whom I am indebted for the privilege of reporting the case.

Dribbling with difficulty in passing urine had been noted since birth. For days there had been intermittent attacks of crying, with fever for 2 hours and convulsions for 2½ hours.

The onset of the present acute illness began 48 hours before admission to the hospital, with attacks of crying, and an associated bulging in the upper end of the scrotum. The mother stated that the base of the penis had always been large, that the patient always had difficulty in passing his urine, that the urine came away in dribbling and that the child had to use considerable force to urinate. For about 24 hours no urine had been passed.

The child had had no previous illnesses. He was one of twins and his brother is normal.

Physical examination revealed an evidently acutely ill, pale child, grunting as if in severe pain. The head, neck, heart, and lungs were negative. The liver and spleen were palpable. A suprapubic tumor was found that extended ½ inch above the umbilicus, due to a full bladder. At the base of the penis was seen a swelling about the size of a crab apple. Both testes were present in the scrotum.

An indwelling catheter was inserted into the bladder and the bladder was gradually emptied. The swelling at the base of the penis persisted.

Temperature on admission was 101 degrees. Examination of the urine (obtained from the indwelling catheter) showed albumin, 3 plus, 50 to 60 white blood cells and 10 to 15 red blood cells per low power field. The phthalein test showed a total output of 42 per cent for 3 hours; blood chemistry showed non-protein nitrogen, 44. The blood count revealed white cells 25,000. The urethrogram (Fig. 1) disclosed a large round shadow in the urethra about the size of a quarter. A lateral roentgenogram showed shadow about inch long.

Pressure on the diverticulum caused the urine to run out of the external urethral orifice alongside the catheter. The diverticulum then diminished in size.

The pre-operative diagnosis was diverticulum of the urethra with complete retention of urine, acute cystitis, and acute pyelitis. Operation consisting of suprapubic cystostomy was advised.

At operation, February 2, 1934, a suprapubic cystostomy was done. Ether anesthesia was used. A No. 14 mushroom catheter was inserted and held in place by a chromic catgut suture. The bladder was closed with interrupted sutures of catgut.

Eight days after the operation the diverticulum became red, swollen and tense, and a pin point opening developed on top of the diverticulum. A diagnosis of infection of the diverticulum was made.

A second operation was done March 3, 1934 (Fig. 2). Under ether anesthesia, pin point opening in the scrotum was enlarged. Several ounces of thick, yellow pus were evacuated from the diverticulum which was then isolated by blunt dissection and amputated just above its entrance into the urethra. A soft rubber catheter was introduced into the bladder and the opening in the urethra was closed in two layers with catgut.

Instead of removing the sac at its attachment to the urethra, it was amputated directly above this point, the small fringe of the neck of the sac being utilized to close the defect in the urethra. The object of this procedure is to prevent the formation of a stricture of the urethra at this point.

The child made an uneventful recovery and was discharged from the hospital on April 10, 1934. Since leaving the hospital a stone has been passed. On chemical examination the stone showed a mixture of calcium phosphate, triple phosphate, and a trace of urate.

ETIOLOGY AND PATHOGENESIS

Many theories have been advanced to explain the origin of this condition. It may be interesting to present briefly some of these theories.

One of the early authors who attempted to explain the origin of diverticulum of the urethra was Vallemier (1865). In his opinion diverticula of the urethra are due to a lack of development of the spongy tissue of the urethra, the condition being similar in many respects to hypospadias, with the difference that in the latter condition the defect includes all tissues of the penis, including the skin.

According to DePaoli (1885) urethral diverticula are due to primary atrophy of the corpus spongiosum, allowing a bulging of the urethra to form a sac on the ventral wall.

Kaufmann (1886) advanced the theory that urethral diverticula result from urinary obstruction in fetal life, the obstruction being caused by a delay in the disappearance of the septum between the penile and glandular portions of the urethra. Thus a delayed union of the two portions of the urethra occurs, the urinary flow being obstructed, causing an expansion of the wall. The valve-like structures described by Hueter are persisting remnants of this septum. These valves are not interpreted as the cause of the diverticulum, but are interpreted as a contributory factor in the increase of its size when once developed.

[1] From the Children's Memorial Hospital, Chicago.

Fig 1 Showing diverticulum of urethra Note presence of catheter in urethra

Petz, quoted by Bokay (1900), states that the diverticulum in his case was due to a congenital stricture of the urethra

Watts (1906) expresses the following opinion as to the origin of urethral diverticula "Since acquired true diverticula are usually the result of obstruction to urination, we should expect such an obstruction to be an important factor in the formation of urethral diverticula in early life Such obstruction in childhood or intra-uterine life may be due to adhesions of the prepuce to external meatus, a congenital narrowing of the preputial orifice, or a congenital stricture of any portion of the urethra"

He then discusses the valve-like structures which occur in the urethra in certain cases and states that they may constitute a cause of obstruction He notes that only in 2 of the cases which he studied (Hueter and Schlueter) could the formation of the diverticulum be ascribed to valves in the urethra In these 2 cases, at operation, a circular valve was found at the outer extremity or diverticulum

He adds that in the case of Hendriksz a valve-like structure was found which was apparently only a thickening of the urethral wall Also, in some cases the valves mentioned as occurring at the anterior and posterior extremities of the diverticulum are merely secondary formations due to undermining of the urethral wall by the diverticulum as it increases in size Bokay (1900) substantiates Watts' theory and states that the valves in one of his cases were formed in this manner Watts has found that such valve-like structures are often present in acquired diverticula, resulting from perforation of the urethra

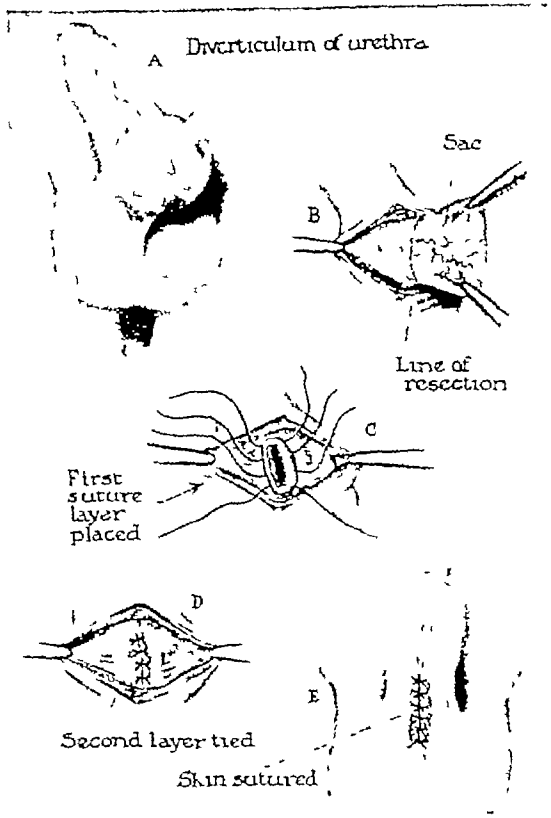

Fig 2 *A*, The diverticulum *B*, Isolation of the sac Dotted line shows point of resection *C*, First row of through-and-through sutures in place The sac has been amputated just above the urethra *D*, Second row of sutures *E*, Suture of skin with fine silk

A very interesting theory regarding the origin of urethral diverticula has been put forth by Suter (1908) He bases his theory on a histological study and concludes that diverticula of the urethra should be regarded as epidermal pockets communicating with the ventral wall of the urethra He explains the embryology of the condition as follows "The urethra originating from the genital furrow is covered with epidermis A canal is formed which occupies the position of the future urethral canal This canal is at first not closed on the side of the ventral surface of the future urethra, and there is a communicating bridge of epithelium connecting with the external skin Normally this epithelial bridge (which remains squamous, while that within the canal becomes cylindrical) is absorbed" It is the persistence of this bridge which, according to Suter, gives the origin to diverticula and also to dermoids (Fig 3)

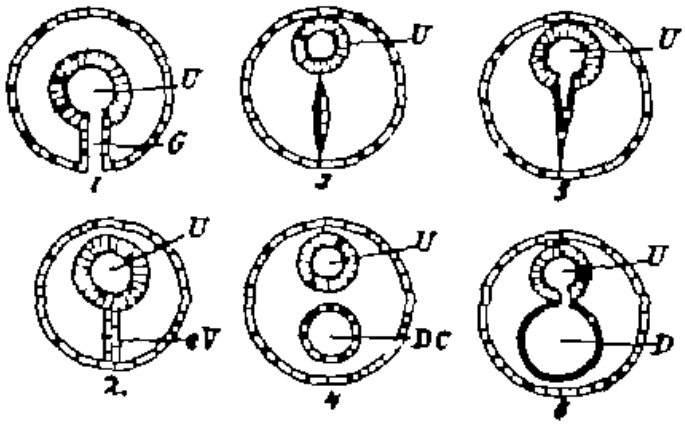

Fig 3 From Suter Showing the urethra, *U* and the genital gutter, *G* 2 Genital gutter closed, bridge of epithelium, *V*, remaining 3, Epithelial bridge disappearing 4 Cystic dilatation of the bridge giving rise to dermoids, *DC* 5 Incomplete closure of the epithelial bridge 6 Dilatation of the incompletely closed bridge of epithelium, gives rise to the diverticulum, *D*

Cabenas (1915) after a review of the various theories of etiology makes the following summary of his conclusions

There is considerable probability that these dilatations result especially as Durand affirms, from a disturbance in the development of the various tissue strata of the urethra, *due to an abnormal blood supply particularly in* the spongy tissue

In other cases, one may invoke not a disturbance but a defect in the development of these strata, the corpus spongiosum being totally wanting in the region of tumefaction This can be explained only by an incomplete closure of the urogenital gutter

3 The presence of a valve in dilatation of the urethra is only to be considered as an adjuvant cause (joining its mechanical action with that of urinary pressure) in defect already formed or on the way to formation

AGE

A review of the literature reveals that 4 cases in which patients were less than 1 year of age have been reported (Busch, Bokay Cabenas, Ternovsky), however only 2 of these patients were operated upon. The case herein reported was 6 months of age thus making it the third patient under 1 year of age who was operated upon

It may be interesting to mention that in Lotzbeck s case the condition was diagnosed as late as the twenty first year although the symptoms had been present since early childhood.

The age incidence is given in the accompanying table.

LOCATION

Congenital diverticula of the anterior urethra occur on *the ventral wall of the urethra. They are* frequently located immediately behind the fossa navicularis and open with a narrower or wider mouth into *the urethra*

Denk states that in 23 cases of congenital diverticula which be gathered in the literature (including his own case) 14 arose just behind the fossa *navicularis*, 7 were *in the* pars cavernosa (prebulbar) and 2 were in the pars bulbosa. Denk observes that the fact that the classical congenital diverticulum of the urethra is situated in the anterior portion is in accord with Kaufmann s theory as to their origin namely that they are due to a retarded establishment of communication between the penile and glandular portions of the urethra.

Drachter states that congenital diverticula of the urethra are for the most part in the penduloua *and scrotal portions and on the under surface of* the urethra.

SIZE

The diverticular pouches are described as varying *in size from a hazelnut to a walnut or pigeon s* egg In the case of Hendrikx (quoted by Watts) the size of the diverticulum was stated as being greater than the capacity of the bladder

CLASSIFICATION

Diverticula of the urethra may be classified as congenital and acquired The congenital diverticula are seen in the anterior urethra and in a large percentage of cases occur in young subjects, or in patients whose history suggesting a urethral diverticulum dates back to early life Movat says that when there is complete absence of any history of colic, thus precluding the possibility that a stone has descended to lodge in the urethra, and when there is no stricture or local lesion likely to give rise to a urethral or a para-urethral stone formation or other lesions to account for the origin, diverticula must be considered as congenital

Likewise we must consider as congenital the cases arising in infants and also in children whose symptoms date to birth.

The acquired diverticula occur for the most part in the posterior urethra and the causes, such as urethral calculus, stricture, perforation of the urethra resulting from injuries or rupture of cysts, do not as a rule occur in childhood.

It has been suggested by early writers that the congenital and acquired varieties are to be differentiated by the fact that the former have a lining of mucous membrane similar in nature to, and continuous with, mucosa of the urethra, while the latter are devoid of a mucosa It is generally admitted at this time that such a distinction is false, since inflammatory processes within a diverticulum may destroy the mucosa

ASSOCIATED PATHOLOGY

The urethral diverticulum not infrequently becomes the site of an inflammatory process caused by the stagnation of the urine within it and by superimposed infection This may lead to a fistulous opening on the surface of the penis

Calculus formation may occur in a diverticulum and in the case reported by Grube in a child of 8½ years, the sac contained 162 small stones Stones were present in Cabezas' case

The obstruction to the flow of urine, caused by the pressure of the filled sac upon the urethral lumen, leads to dilatation, infection, and destruction of the upper urinary tract

In the cases which have come to autopsy (Bokay, 2 cases, Ternovsky, Frontz), the effects of urinary stasis were evident in hydro-ureter, hydronephrosis, pyonephrosis, and pyelonephritis

SYMPTOMS

In some of the cases the diverticulum could be emptied completely by pressure only to fill up again subsequently In my case it was possible to empty the diverticulum completely by the introduction of a catheter into the diverticulum Pressure upon the tumor in my case discharged purulent fluid (urine and pus) at the external meatus

However, when diverticula become infected, certain changes occur in the tumor, namely, the skin becomes red and the diverticulum becomes attached to the skin, perforation of the skin with discharge of urine and pus soon occur This train of events *occurred in my case*

Although complete retention of urine is rare, this symptom was the direct cause of the patient's admission to the hospital in the case reported in this paper The retention is mechanical in origin The presence of the large diverticulum causes pressure upon the urethra, hence complete retention follows

The outstanding clinical finding in this condition and one which occurred in every case which we have studied, is a tumor of the ventral surface of the penis This tumor appeared in some cases during urination and in others is described as increasing in size during urination In most cases it is noted that pressure on the tumor caused urine, or watery pus (in infected cases) to issue from the external meatus, and at the same time the tumor would diminish in size.

As a rule, the tumor is not attached to the skin and is generally described as being freely movable laterally, it is not tender on pressure nor are there external evidences of inflammation

Disturbances of urination are encountered in the form of incontinence, or dribbling due to slow emptying of the pouch, difficulty, a small stream, or the passing of urine by drops In the case of Laugier-Anger (cited by Watts after Guyon) the patient voided normally, but the pouch filled first and then the stream appeared

In the cases of Hendriksz and Lotzbeck, Watts states that the urine was never voided in a stream All the urine entered the pouch and was emptied by pressing the pouch with the fingers

Nicholson states that in the absence of infection and urinary obstruction, it is quite possible for diverticula to be non-productive of symptoms Especially is this true of smaller ones which readily empty and are thus free of stagnating urine

DIAGNOSIS

As a rule the diagnosis of diverticulum of the anterior urethra is relatively easy In my case the diagnosis was based upon the following

1 The presence of a soft fluctuating tumor on the ventral surface of the penis

2 Pressure upon the tumor was followed by a discharge of urine and pus at the external urethral orifice with a complete disappearance of the tumor

3 Associated disturbances of urination, and finally complete retention of urine, necessitating the use of an indwelling catheter

4 Diagnosis was verified by urethrogram (Fig 1)

PROGNOSIS

The prognosis in these cases is entirely dependent upon the extent of the pathological changes which the diverticulum has caused in the upper urinary tract through obstruction and ensuing infection, and this means early diagnosis and early surgery before the onset of irreparable damage to the upper tract.

When the patient is operated upon before urinary stasis has caused serious damage to the upper urinary tract, the prognosis is good This is seldom the case when the operation occurs after the urinary tract has been damaged

TREATMENT

Excision of the diverticulum is the best form of treatment in this group of cases Invagination of small diverticula may be tried, but as the majority of patients have large sacs, the invagination is not feasible. Moreover, invagination of a large sac may produce urethral obstruction The relative ease and simplicity of diverticulectomy and the fact that excision removes the sac once and forever, justifies the statement that excision of the sac is the method of choice

DIVERTICULA OF THE ANTERIOR URETHRA IN MALE CHILDREN

Author Date	Patient's age	Symptoms	Duration of symptoms	Method of diagnosis	Location	Treatment	Result	Remarks
Hendricks (quoted by Watts) 1897	8 yrs.	Tumor on lower surface of penis, distended during micturition. Pressure with fingers emptied the sac	Not stated	Inspection	Lower surface from fossa navicularis to penoscrotal junction	Excision of diverticulum and closing of valve into fossa of navicula. Lined at anterior end posterior opening of urethra into the pouch	Good	
Leisebach (quoted by Watts) 1882	yrs	Pouch at lower border of penis below scrotum. After micturition pouch collapsed and penis was normal in appearance	Since early childhood	Inspection and introduction of catheters	Low at border of penis	Operation refused	Not stated	
Lemper Auger (cited by Watts after Guyon) 1884	3 yrs	Tumor on lower wall of urethra. Lined mucous membrane along inferior wall caught in pouch	Since birth	Inspection and introduction of sounds	Fossa fossa navicularis to middle of penile urethra	Excision of pouch 3 years later by Vulliamoz	Not stated	Pouch lined by mucous membrane. The surgeon spontaneous closure. There was no valve at junction of pouch with urethra
Busch 1884	4 mos.	Pouch on under surface of penis	Since birth	Inspection and sounds	Under surface of penis	At months diverticulum was incised and edges sutured to skin. Subsequent attempt to repair by Busch	Not stated	
5 Grube 1887	8½ yrs.	Swelling on under surface of penis at penoscrotal furrow	18 mos	Inspection	Under surface at penoscrotal furrow	Removal of stones from bladder and from diverticulum. Diverticulum not excised but the edges of the urethral orifice were freshened and sutured	Healing	Diverticulum contained rice small stones. Grube considered it congenital in result of faulty closure of valves of the urethral orifice, containing shallow cavity in floor of urethra in which stones lodged, giving rise to urinary obstruction, new stone formation and progressive dilatation of the urethra
6. Hosing 1889	4 yrs.	Dribbling of urine. Tumor on under surface of penis	Since birth	Inspection and introduction of catheter into pouch	Under surface from fossa navicularis to scrotum	Excision of diverticulum and valve	Good	Dribbling was first attributed to paralysis of bladder. Another physician thought it was due to a narrowing of prepuce at orifice and stretched the orifice. Hosing explained it as due to valve-like closure of the urethra
7 Schlenter (quoted by Watts) 1897	10 yrs.	Dribbling. Tumor on under surface of penis. Tumor collapsed when emptied with catheter	Not stated	Inspection	Fossa navicularis to scrotum	Excision of diverticulum and valve into fold of mucous membrane which were at anterior extremity of diverticulum	Good	
8 De Paoli 1898	14 yrs	Swelling on under surface of penis. Reached size of hen egg on straining	Not stated	Inspection	Under surface of penis	Partial excision	Not stated	Considered due to weakness in urethral wall with dilatation, result of primary atrophy of corpus spongiosum
9 Case (quoted by Bakey) 1899	3 yrs.	Tumor of penis. Difficult micturition. On catheterization obstruction met at 3 to 4 cm from meatus	years			Pouch opened and edges of valve commencing with mucous membrane and sutured	Healing	Case considered than case of congenital stricture of urethra which had caused dilatation of urethra and diverticulum
10 Bakey Case 1899	3½ yrs.	Difficulty dribbling, retention, swelling of penis on straining to know whether the sac of pouch's size	3 weeks	Inspection and catheterization with catheter	Lower surface of urethra	Operation postponed due to poor condition. Lacerations of urethra and bladder. Constitutional treatment	Lower operation and death after about month	Autopsy showed evidence of stricture and pulmonary in bladder, kidneys, and ureter. On lower wall of urethra opening from external meatus was an oval opening 14 mm. leading to diverticulum (size of pouch) and by fistulous tract was continuous with lumen of urethra

DIVERTICULA OF THE ANTERIOR URETHRA IN MALE CHILDREN—Continued

Author Date	Patient's age	Symptoms	Duration of symptoms	Method of diagnosis	Location	Treatment	Result	Remarks
11 Bokay Case 2 1890	3 wks.	Difficult urination Continual dribbling Soft fluctuating tumor on under surface of penis Pressure on tumor caused flow of urine at meatus	Since birth	Inspection and catheterization	Lower floor of urethra near fossa navicularis	Operation for phimosis Operation for diverticulum refused	3 months later, death seemed imminent	
12 Bokay Case 3 1890	3 yrs	Dribbling, frequent painful urination pyuria Tumor size of hazel nut on lower portion of penis near penoscrotal junction became size pigeon's egg on urination and emptied on pressure of fingers	1½ yrs.		Middle of pars cavernosa urethra	Excision	Death after 2 months	Autopsy showed dilatation of kidneys and ureters
13 Durand (quoted by Watts) 1901	2 yrs	Tumor on under surface of penile urethra	Not stated	Objective findings	Communicated with urethra by an orifice 1 cm in length 1 cm. from external meatus	Excision	Not stated	All coats of urethra including spongiosum were represented in wall of pouch
14 Escat 1908	5 yrs.	Fluctuant tumor of lower border of penis	Not stated	Not stated	Penile urethra on ventral surface	Extirpation	Recovery	
15 Habercan 1911	8 yrs.	Tumor on under surface of penis increased in size during urination Slow, small urinary stream	Not stated	Objective findings	Lower surface of urethra, from behind fossa navicularis to middle of pendulous urethra	Excision	Good	
16 Denk 1912	8 yrs.	During urination a balloon formed on under surface of penis. It emptied by slow dribbling after act of urination was completed	Noted soon after birth	History and objective findings	Began behind glans and involved two-thirds length of penis	Extirpation	Excellent	
17 Cabezas Case 1 1913	In 1st yr	Tumor on under surface of penis during urination Did not empty completely and urine could always be expressed from it	Since birth	Objective findings	Ventral surface of penile urethra	1 Artificial hypospadias 2 Resection of diverticulum 4 years later	Good	Resection not done when first seen due to poor general condition Seen first under 1 year of age Operated at 5 yrs.
18 Cabezas Case 2 1913	14½ yrs	Recurring attacks of retention Tumor of penis, size of walnut	Since 4 yrs of age		Cavernous urethra	Excision	Not stated	Diverticulum contained a large number of small calculi
19 Fernovsky 1930	10 days	Tumor at root of penis Pressure on it caused urine to exude at external meatus. Disappeared when catheterized and returned an hour later	Since birth	Inspection and palpation Verified by urethrogram	Under surface of penis at border of scrotum	No operation	Death	Autopsy findings Hypertrophy of bladder wall, cystitis, hydroureters, pyelonephritis and pyelonephrosis
20 Frontz 1931	14 mos	Soon after birth, urinary obstruction Tumor visible beneath scrotal skin Pressure on this gave escape of watery pus at external meatus, and collapse of tumor	Noted soon after birth	Autopsy	Diverticular orifice (2 cm. in diameter) on inferior wall of mid bulbous urethra	No surgery attempted	Death from uremia a week later	Autopsy findings Valve-like fold at the entrance of the diverticulum which allowed urine to distend the sac but prevented its emptying When the sac was distended the bulbous urethra was compressed from below upward Extreme hydroureter, hydronephrosis and pyonephrosis
21 Kretschmer 1935	6 mos.	Difficult urination Swelling on under surface of penis Complete retention	Since birth	Inspection and palpation Aspiration with catheter Urethrogram	On left side of penoscrotal junction	Diverticulectomy	Cure	

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EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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MARCH, 1936

CANCER AND PUBLICITY

PUBLICITY in the fight against cancer acts as a two-edged sword It points the way to the prevention and to the early treatment of cancer in all its forms It stimulates the hope that the public may be made conscious of bodily abnormalities or irregularities which should be investigated It provides the opportunity for physicians to inform the people of the known and tested methods by which these diseases may be combated If the agencies which supply such publicity would stick to "fighting cancer with facts," the good which they could accomplish would be immeasurable There is a painful tendency, however, not only to supply the facts, but also to pass on as facts, the new untested fancies because of a quality they possess which is known as "news value"

It is this unfortunate feature of the publicity in dealing with the cancer problem to which we should give particular attention The news agencies, which are the worst offenders, seem to get especial satisfaction in ferreting out, old, discarded forms of treatment These are dressed up as great unheralded discoveries and fed to the long suffering public Thus, within the last 6 months one of our smart weekly magazines has given artificial respiration to at least three prostrate "cancer cures" It has propped them up and supported them with its rhetoric, at the same time making witty, slurring remarks about the organized medical profession which saw fit to reject these discoveries The news agencies will frankly admit that they are interested in gathering and publishing anything that is news They will point out that the public interest in cancer has been aroused and that cancer stories make good headline features People are anxious to hear about work in this field If it is explained to news men that the cancer problem is one of great difficulty, that scientific men have spent their whole lives on single special parts of the problem, that great institutes have been established throughout the world where coordinated organized research is being conducted by expert specially trained investigators, that cancer comprises a large group of different diseases with as great differences between them as typhoid fever is different from measles, that, even in regard to the infectious diseases, nobody is foolish enough to look for one "single cure" for all of these infections at the same time, even if the problem is made as clear to the news agencies as it can be stated, there will still appear the alluring headline—"Backwoods doctor discovers cure for cancer" This hardy plant, though not an an-

mal, appears at least as a biennial. It is too much to expect that the news men will confine their attention only to "all the news that's fit to print." It is too often apparent that fitness as such does not enter The great need of the news agencies at the present time is *the development of a desire for accuracy and for a conscience.* These apparently harmless headlines are usually the cause for the movement of a caravan of helpless sufferers toward a forlorn hope. They go at no matter what sacrifice, regardless of the distance. They pour out their life savings expecting the miracle which the papers have promised. The mass psychology buoys them up for a time. Then, failure and despair The excitement over the newspapers turn to other more sensational items. The failure which would also seem to have "news value somehow never gets mention. The papers sometime could at least tell us where are the cures of yesterday which crowded all these poor people about the shrine of the discoverer

The whole fault with this unwholesome cancer publicity is not entirely with the news agencies. The scientific investigators must also share a part of the blame. Any scientist who is conducting studies on any phase of the cancer problem should be unusually careful in what he publishes The very anxiety of the news reporters will frequently cause them to misinterpret or to exaggerate the claims of the scientist. Scientific reports should clearly state that the experiments so far have been carried out only on animals. If the results seem to warrant a trial in human cancer it should be easy to get some of the reputable medical schools or cancer research institutes to co-operate. This would in no way detract from the credit of the investigator It would only tend to prove that the scientist had an honest belief in his remedy It would indicate that he wished corroboration from unbiased observers. This is the way that insulin was introduced to the medical profession by Dr Banting. He did not insist that his remedy be kept secret. He did not start a procession of diabetics to Toronto He quietly asked several of the leading medical school clinics to try out his agent against diabetes. This did not take any of the glory from the greatness of his discovery It simply proved quickly that he was right. The same would be true in regard to any proposed treatment for cancer When the scientific investigator gives an interview to the press before his discovery has been reported through regular medical channels, it lays him open to criticism on at least two counts. It shows a disregard for the other members of his profession who by right should know of new developments in medicine before the general public does. It is only fair that physicians who will be called upon to advise their patients should have a chance to think about the new treatment. It furthermore shows a naive simplicity on the part of the discoverer who thinks he can make such an announcement and escape the consequences. It makes the more cynical members of society look upon it as a desire to meet the consequences at any price—provided it is high enough. The cancer research worker must be patient painstaking and deliberate. He must possess balanced judgment. He must subject his results to critical analysis. He must not let his enthusiasms bias his opinion. He must make his mind control his emotions. He must not jump to conclusions before he has tested and retested his results. When it is recalled how many apparently sane investigators have gone wrong on the cancer problem, it is evident that this field is full of pitfalls. Even the head men of cancer institutes have made mistakes in backing and promoting some of the seeming discov-

eries of their staff The fault in such instances is in assuming more than the results have warranted The repeated disappointments in cancer cures naturally have made authorities in this field very skeptical about new discoveries They wish an opportunity to try them out before accepting them at face value This is in a way unfortunate It perhaps may make a slower acceptance of some fundamental discovery which may unlock the doors to progress It also makes the tyro believe that these men are prejudiced against any new line of investigation He consequently develops a martyr complex, which unhappily is fostered by the many agencies The embryo scientist is pictured as a St George fighting against the dragons of organized medicine

In reality, the cancer authorities are simply trying to protect the public against exploitation The appeal made by the new discovery attracts a large proportion of the public. The mass of the people accept it because of its emotional appeal, the intellectuals, because they are constantly on the alert for the new The latter group are often more deceived than the former They lack the proper background to make a reasonable estimate The public, consequently, is also partly to blame for the uncontrolled publicity given to the cancer problem If the public would react in some sensible way to these announcements instead of accepting them as reported, progress would be made If the public would demand that the news agencies back their statements by the endorsement of recognized authorities in the field, or that the news of medical items should be handled through a publicity committee of the county medical society, if it could be made uncomfortable for those who broadcast false information, or if all the people would refuse "to be fooled all the time" by the papers but would receive their misinformation with jeers and ridicule, — there might be a more honest attempt to get information of value rather than for its sensational qualities The news of cancer would not in itself have malignant qualities as it does now when "it serves no useful purpose"

JOHN J MORTON

APPLICATION OF FIXED TRACTION FOR TRANSPORTATION OF PATIENTS WITH FRACTURES

THE United States census reports show that there were 36,000 fatalities from automobile accidents in 1935 It is estimated from reliable figures that there occurred one million fractures during this period from the same cause

Sir Anthony Bowlby, head of the medical department of the British Expeditionary Forces during the early part of the World War, estimated that the mortality from compound fractures after the adoption of fixed traction in transportation was reduced from 80 per cent to 20 per cent The stretcher bearer and the doughboy were trained to apply fixed traction on the battle field It is now more than 17 years since the World War and we are not giving our ever increasing number of sufferers from high speed locomotion the same chance of life and health that was given our soldiers During that time many more Americans have been injured or accidentally killed than in all the wars in which the United States has engaged

It has been argued that the layman should not be taught to apply a splint for aid in transportation because of the implied entrance of the laity into the medical field Nevertheless, no one would argue that a layman should not attempt artificial respiration in a case of submersion, or that a layman should not apply a tourniquet to prevent death from hemorrhage, provided a doctor were not available Doctors are rarely present at the time

of an automobile accident. If by the application of a Keller Blake splint to the lower extremity or a Murray Jones splint to the upper extremity jackknifing of the fractured bones with resultant shock and delayed union can be prevented and the patient transported in safety to the nearest doctor or hospital for treatment, a great step in advance will be made.

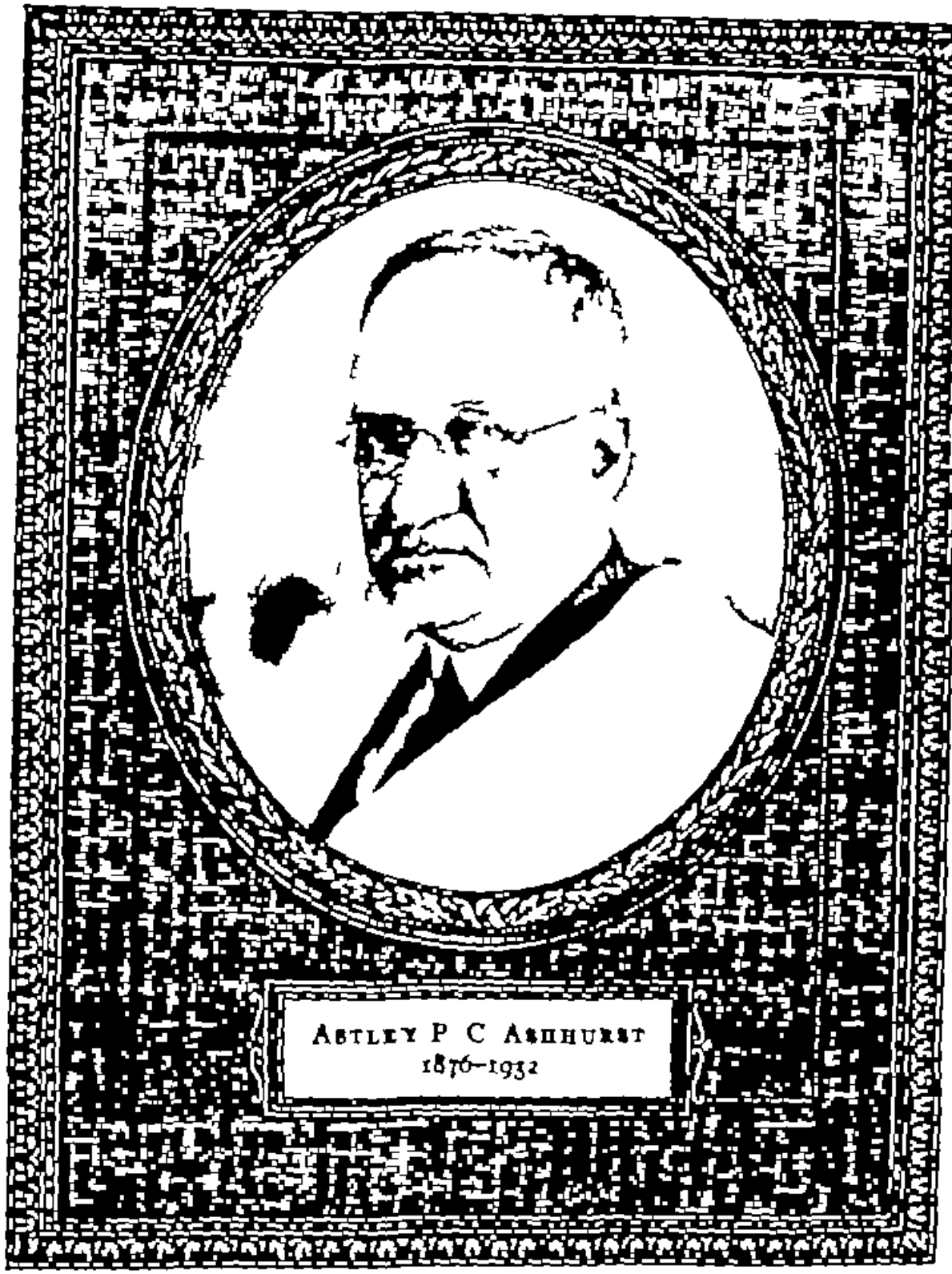
By medical and lay propaganda in many cities and states, the Committee on Fractures of the American College of Surgeons, through its regional groups, has stimulated interest in the safe transportation of fractures, and definite improvement is noted in many localities. Ambulances in general are manned by doctors, fire or police departments, or morticians, according to the section of the country. Instruction is being given to these various groups and many ambulances are now equipped with traction splints, but unfortunately only a comparatively small proportion of them has been reached.

The American Red Cross has been interested for a long time in the problem of emergency first aid along automobile highways. Instruction in the application of the Keller Blake half ring splint for fractures of the lower extremity has been incorporated in the latest edition of its book on first aid. It is now establishing emergency first aid stations along many of the main highways. Traction splints are a requirement in the equipment of these stations, and their attendants are being trained in the application of immediate traction. The Committee on Fractures of the American College of Surgeons is co-operating with the American Red Cross by asking the members of its Regional Fracture Committees to assist in the necessary instruction to be given the attendants. There are at present 238 stations fully equipped and operating, and 1,440 are promised to be opened within the next 6 months. These stations are being started in 34 states.

The officials of the Boy Scout organization have taken up very actively the problem of transportation of the injured and, in all the camps throughout the country the Boy Scouts are being trained in the application of fixed traction. The leaders of the Girl Scouts have indicated their willingness that similar instruction be furnished the girls.

The American College of Surgeons, having entered into this move to protect the traveling public, has assumed certain obligations. With the large amount of lay propaganda that is being disseminated by the American Red Cross, the Boy Scouts and the Girl Scouts, it is necessary that surgeons throughout the country should be themselves thoroughly informed of the method of applying fixed traction and should be willing to offer their services to aid these organizations should they be so requested. If these requests come from the American Red Cross it is advisable to follow the method described in the Red Cross book on first aid. There can be no question that if transportation of patients suffering from fractures can be so improved injury incurred during transportation will not be added to the original injury the saving of life, and the decrease in the period of hospitalization will be of great economic benefit to mankind.

Frederic W. Bancroft,
Chairman, Committee on Fractures
American College of Surgeons



Astley P C Ashhurst
1876–1932

MASTER SURGEONS OF AMERICA

ASTLEY PASTON COOPER ASHHURST

FROM Colonial days Philadelphia has contributed more than its share to the progress of medicine Soon after the middle of the eighteenth century a group of young Americans returned from Edinburgh imbued with the spirit of that school It was not long before Morgan and Shippen started the first medical school in Philadelphia, and were soon joined by Kuhn and Rush Since that time there has been a steady stream of men whose writings and teachings have spread throughout the land the results of their own searchings after truth Bond and Barton, Wistar and Physick, the Hares and Woods, the Hodges and Penroses, Agnew and Leidy, the Peppers and Ashhursts

Astley Ashhurst early appreciated the responsibilities he had inherited from his father, John Ashhurst, Jr , professor of surgery at the school Morgan had started His devotion to this profession and its ideals was the dominating influence in his whole life Except for his war service, his entire career was spent in Philadelphia He was born there August 21, 1876, his mother being Sarah Stokes Wayne Ashhurst He prepared at the Forsyth School, now the Episcopal Academy, a private college preparatory school located in Philadelphia, and entered the University of Pennsylvania from there, receiving his degree of Bachelor of Arts in 1896 and his Doctor of Medicine in 1900 His classmates always remembered him as taking prizes in Latin and Greek and in taking senior honors in the Academic Department, and he was elected to membership in the Philomathean Society, the Phi Beta Kappa and the Sigma Xi fraternities, and graduated the first man in the senior class of the medical school

After leaving the medical school he served an interneship from 1900 to 1901 at the Children's Hospital, and from 1901 to 1904 at the Episcopal Hospital Following his interneships he served an apprenticeship in the dispensaries of the Episcopal, Orthopedic, Children's, German (now Lankenau), and the Pennsylvania Hospitals until 1913, when he was elected surgeon to the Orthopedic Department and associate surgeon to the Surgical Department of the Episcopal Hospital In 1914 he was appointed surgeon to the Orthopedic Hospital and in 1915 he was promoted to the position of surgeon at the Episcopal Hospital His training as prosector to Dr G G Davis, professor of applied anatomy at the Medical School of the University of Pennsylvania, gave him a knowledge of

surgical anatomy which not only influenced his operative work, but hallmarked all his contributions to surgical literature. For 19 years, 1911 to 1930, he was an instructor in surgery at the University of Pennsylvania teaching operative surgery on the cadaver From 1930 until his resignation in May 1932 he was professor of clinical surgery at his Alma Mater

From the establishment of teaching in the University's Graduate School of Medicine, in 1918 Dr Ashhurst evinced great interest in the ideas and work of the School In 1920 he became an associate in surgery in the School, in 1921 an associate professor of surgery and in 1923 a professor of clinical surgery The latter post he retained until his death, in 1932—although inactive from illness toward the end. His teaching of clinical surgery to the graduate students of surgery especially in the Episcopal Hospital of Philadelphia, exemplified those qualities of conscientiousness, erudition, and technical perfection which were his admirable characteristics.

His wide knowledge of surgical literature and his mastery of the fundamentals of surgery together with his interest in teaching, made his lectures and quizzes popular with the students. The student's first impression of him was usually unfavorable. His hesitating speech, which was the result of stuttering in early manhood, together with his hypercritical respect for the truth were causes of his being at first misunderstood, but his sterling character and the justice of his criticism not only of others but of himself were soon appreciated by the students, and explains his popularity with them.

"As a surgeon he was methodical in the superlative degree," says Dr Crossan, one of his associates, and insisted upon performing every detail of the operation himself including the application of the bandages. Neither brilliancy nor speed in operating was attempted by him and he seemed to abhor the spectacular He was just as meticulous of the pre-operative and postoperative care of his patients as in his operative technique, and he would never accept the opinion of any one without himself consulting the evidence, making his own physical examination, examining the X ray films and studying the gross microscopical preparation of the tissues."

He was proud of being a general surgeon and with such wide and varied training as he had received he was well fitted for such a broad field. Though tempted, after the death of Dr G G Davis, to limit himself to orthopedic surgery for which he had such an unusual training, he said that surgery of the bones and joints belonged to the general surgeon and that such a special field was too small to occupy the full time of a well trained surgeon. He was trained also in gynecology For several years he did the neurosurgery at the Orthopedic Hospital.

Outside of Philadelphia, as one would expect he was probably best known as an author His scientific articles were not only clear and simple but uniformly accurate, and all of his contributions to surgical literature reflect his scholarly

attainments As one would expect from his clinical work, he never accepted the statements of others in literature, but always ran them down to their source and frequently embarrassed his colleagues by his discovery of inaccuracies One wonders where he found time for all this work, for between the years 1902 and 1920 he wrote 82 magazine articles, was co-author in 10 others, wrote numerous book reviews, edited 2 volumes of the Episcopal Hospital Reports, was a co-author of 2 textbooks (*Enlargement of the Prostate*, with Dr John B Deaver, and *Surgery of the Upper Abdomen*, with Dr John B Deaver) and published the first edition of his book *Surgery, Principles and Practice*, and the "Gross Prize" essay "An Anatomical and Surgical Study of Fractures of the Lower End of the Humerus"

He was a very active member of the Philadelphia Academy of Surgery and was rarely absent from its meetings His presence was not passive in any sense, but always active up to the time of his illness This activity consisted not only in his own presentations, but in a critical discussion of nearly every paper He felt it the duty of every Fellow to prepare a discussion of the subjects presented at the meeting His knowledge of the literature and careful preparation of his discussions stirred his fellow members to efforts usually beyond their inclinations They all knew that he would be at the meeting and that he would make as great if not greater preparations for his discussion than they had in their presentation His value to the Philadelphia Academy of Surgery cannot be overestimated He delivered the annual address in 1910 and served as president in 1928 and 1929, and received the Samuel D Gross Prize in 1910 for "An Anatomical Study of Fractures of the Lower End of the Humerus"

He was vitally interested in the College of Physicians and could be found in the building at some time during each day reviewing literature or discharging his duties as honorary librarian, a position he held from January 9, 1928, to the time of his death

He was elected a Fellow of the American Surgical Association in 1913, and he brought to that association the same unique qualities which he exhibited in the Philadelphia Academy of Surgery Astley P C Ashhurst could not be other than Astley P C Ashhurst—whether it was in Philadelphia, in the American Surgical Association, the Interurban Surgical Society, the Society of Clinical Surgery, the Society of Military Surgeons, the International Society of Surgeons, Association de Française de Chirurgie, the Academy of Natural Sciences, or the Historical Society of Pennsylvania, he was the same sterling scholarly character in search of medical truth

His sense of duty and his belief in the obligation of service sent him to the first Officers' Training Camp organized at Plattsburg, in 1916 With America's entry into the World War he organized the Episcopal Hospital Base Unit 34 and was its first medical director. He was sent to France with this Unit December 15, 1917, and returned to America in 1919 In France he served at the front with

the French and the Americans, and after the Armistice was appointed as a consultant to the Hospital Center at Savenay Upon returning home he was appointed chief of the surgical service at the Walter Reed Hospital where he served until the time of his discharge from the Army April 16 1919. He entered the Army as a first lieutenant and was discharged as a colonel He received a citation for "exceptionally meritorious and conspicuous service with Base Hospital 34."

"As a man he was almost a crusader for honesty and truth." With Ashhurst there was not such thing as a white lie or a gray lie. Truth permitted of no comparison and it was either a truth or a falsehood. Few of us have not winced at his criticisms and book reviews, which were rarely sought by writers or publishers because he insisted on recording what he believed to be true His probity won him great respect even though it did not make him popular His was a life devoted to surgery He had no hobbies and his relaxation was study Eventually the long hours of clinical work and study began to show their effects. In 1929, at the early age of 52 he began to suffer from dizzy spells and in the latter part of May 1930 while driving his car on the Roosevelt Boulevard he had his first attack of cerebral thrombosis and crashed into a tree. He was able, however after getting out of the wreck, to take a picture of it and make his way to his office by trolley and bus. Several hours after he reached home it was noticed that he had a left hemiplegia. After months of rest he entirely recovered the use of his hand and leg and gradually returned to operating and teaching However in the latter part of August, 1932 he had a second attack of thrombosis, from which he rallied but a third attack on September 16, 1932 resulted in his death 3 days later To those who knew him intimately he never made the slightest complaint or lament of his misfortune. When asked if he did not know that he was carrying high blood pressure he replied, "Yes but what is there to do about it?"

On July 16 1930 he married Anna Campbell, during his remaining days his constant companion and devoted attendant. His wife and daughter survive him.

Ashhurst was not an ordinary man. He was rather tall but stooped shouldered strong but gentle never hurried but constantly active apparently slow but accomplishing much, seemingly a crabbed bachelor but with a warm heart and understanding sympathy a caustic but fair critic, dogmatic but open minded not widely popular but much beloved, a diligent student all his days and a teacher of sound surgery For over 30 years he met his inherited responsibilities and carried on the Philadelphia tradition. He contributed much and will be sorely missed by his patients, his students, and his friends. WALTER ESTELL LEE.

WILLIAM DARRACH.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

As a result no doubt of the disordered political and economic conditions throughout the world, there has been a dearth of original and enlightening radiological contributions in the field of diagnosis

As in the former volumes of the *Year Book of Radiology*,[1] the authors again present concise, yet adequate reviews of articles which have appeared in medical literature during the preceding year The material has not been selected from the radiological journals alone, but from the many periodicals covering the field of medicine and surgery Many articles which appeared in European literature have been used. Barring the inversion of two or three, the 454 illustrations are well reproduced

The first 303 pages of the volume are devoted to the field of radiological diagnosis Although there have been no spectacular new developments, the articles have a quality which points to a high and efficient plane of diagnosis Arteriography has become a helpful diagnostic procedure More accurate roentgenographic study of the petrous bone has proved to be very valuable

Economic conditions have interfered considerably in the field of cancer research and investigation While no startling new results have been reported, the work in the United States has been carried on with renewed vigor The field of radiotherapeutics covers 195 pages of the volume Included in this section is not only material on radiotherapeutics but numerous articles on other phases of the cancer problem such as etiology Although there is a definite tendency toward increased voltage, its value has not yet been answered by experience The same statement may be made concerning the efficacy of a big radium pack rather than the smaller unit The protracted method of treatment along the lines advocated by Coutard has definitely proved its value, particularly in carcinoma of the upper respiratory tract The value of radiation in the treatment of various benign conditions, such as infections, is gaining much favor

The radiologist will find the volume very valuable as a handy source of reference The satisfactory manner of presenting the material is commended and the volume is recommended to the busy physician not able to read the vast amount of material covered.

The 1935 volume[2] provides the radiologist with a handy source of reference to the important radiologic literature of the year The volume is larger and contains more illustrations than the 1934 review All phases of radiology, both diagnostic and therapeutic, have been covered As in former volumes, the short, concise editorial comments concerning the articles which are abstracted enhance their value

Part I, covering 338 pages, is devoted to the field of radiological diagnosis Recent work in the roentgen study of the nervous system has been rather extensively abstracted The value of thorotrast in the diagnosis of inflammatory foci in bones is of interest. Technical procedures such as "polisography," tomography, and kymography are gaining more attention Other works of interest include various methods of localization of foreign bodies in the eye, breast radiography, serial bronchography, more accurate small intestine studies demonstrating inflammatory lesions and Meckel's diverticulum, refinements in cholecystography, diagnosis of placenta prævia by cystographic studies, pelvimetry and cephalometry and the non-surgical reduction of intussusception under fluoroscopic control. Especially timely, and of great interest to the radiologist, is the increasing tendency of widespread practice of medicine on the part of the hospitals Articles dealing with industrial hazards, the medicolegal aspects of silicosis, and the economic problems of radiology are pertinent

The field of radiotherapeutics is covered in Part II, consisting of 237 pages The death rate due to cancer is increasing Research work on the causative factors of cancer has been carried on with interest Surgery and irradiation remain the most effective weapons at our disposal for combating the disease

Advancements have consisted of attempts toward perfection of irradiation methods based on more extensive experience The question of whether super X-rays are superior to those generated by the 200 kilovolt apparatus or the large radium pack, has not been settled. The various safe-acting safeguards of X-ray apparatus has been an important development. The shift to radiation rather than surgery in the treatment of cancer of the cervix has been an important advance Recent work on the treatment of cancer cases with cobra venom showed it to be ineffective and to have no value in relieving pain. Radiation has gained increasing favor in the field of

[1] The 1934 Year Book of Radiology Diagnosis. Edited by Charles A. Waters, M D, Therapeutics. Edited by Ira I Kaplan, B Sc. M.D Chicago The Year Book Publishers, Inc., 1934.

[2] The 1935 Year Book of Radiology Diagnosis. Edited by Charles A. Waters, M.D Associate editor: Whitmer B Firor, M.D Therapeutics. Edited by Ira I. Kaplan, B Sc., M.D Chicago The Year Book Publishers, Inc., 1935

benign conditions. It has proved to be of real value in the various inflammatory conditions as well as in cases of endocrine disturbances.

The volume should not only be a valuable addition to the library of the radiologist, but to the busy physician or surgeon who does not have time to read the vast amount of material covered.

EARL E. BARTH

ANOTHER Oxford medical monograph[1] embraces in 170 pages a careful review of the literature and a correlation of the now accepted facts. The reference material is worthy of especial comment. The chapter on physiological and pathological considerations is indeed worthy of note. The indications and methods for administering oxygen by different routes in different diseases has been considered on an obviously unbiased basis. Illustrations and clinical problems showing defects as well as success round out the material so as to render it very useful to the general practitioner.

The manner and methods compare favorably with those in use in America. American references and equipment play a prominent rôle in this volume. The authors are enthusiastic for the proper use of oxygen as are all who are familiar with its clinical application. *They offer a hope for the early general* adoption of an "oxygen service" which may be conducted on a voluntary basis and available to all alike. An excellent book bringing up to date the known facts relative to oxygen and carbon dioxide therapy.

M. HERBERT BARKER.

THE book[2] entitled *Apparatus and Technique for Roentgenography of the Chest* by Weyl and Warren, is a highly technical work comprising material dealing with the physical phenomena underlying roentgenography in general, the available roentgenographic equipment and its limitations, the practical application of such equipment for chest roentgenography, and methods of measurement and standardization of roentgenographic apparatus and technique. The authenticity of the work is attested not only by the institution from which it emanates, but also by the stamp of approval given by such men as Dr. Maurice McPhedran and Drs. Chamberlain and Pancoast.

There are doubtless numerous physicians who have become the possessors of roentgenological equipment whose major qualification for operating the apparatus consists in their possession of it. These physicians usually leave the actual technical operation *of their equipment* to technical assistants whose training has usually been skimpy and all too brief and their preliminary groundwork so lacking in mathematical and physical instruction they would find the mastery of this work rather tough going. Most radiological specialists are quite familiar with these principles and practice them in their current medical activities. Other physicians who essay the roentgenological examination of the chest would do well to study this excellent manual.

JAMES T. CASE

IN a small book of approximately 170 pages divided into ten chapters and an appendix, Tucker discusses injuries and their treatment. The appendix is devoted to the illustration of apparatus for the application of diathermy and radiant heat.

Judging from the preface and from the type of illustration used throughout the book, one concludes that the book is written principally from an experience based on athletic injuries. Soft tissue (muscle, tendon, ligament) injuries are dealt with for the most part, and bone, nerve, and visceral injuries are mentioned only in passing. In this regard the title is somewhat misleading. The book can hardly be regarded as a thorough work because so many subjects are touched upon in such a limited number of pages.

In general it would seem that the book would be more valuable in the library of an athletic trainer or a physiotherapist than in that of a surgeon.

JAMES K. STACK.

OUR ideas pertaining to tuberculosis and particularly as regards its treatment have been in such a stage of flux during the past 10 years that a work on this subject at this time compiled from the experience of thirty-four specialists in its various phases comes to the medical profession at an opportune time.

Clinical Tuberculosis[3] is much more comprehensive than its title would infer. The two volumes contain 43 chapters and in each of these the disease is attacked from a different aspect, with ample bibliographies at the end of each chapter. Epidemiology, pathology, physiology, classification, physical diagnosis, X-ray interpretation, symptomatology, medical treatment, surgical collapse, extrapulmonary tuberculosis, complications, etc., are covered in excellent detail. One might be carried away by the enthusiasm of Coryllos in his policy of delay while *acclaiming the virtues of* surgical apical collapse. There are still not a few who might question his early policy of waiting and not applying more simple surgical procedures while endeavoring to ascertain the character of the disease. His ideas are rather at variance with recent teaching which stresses early diagnosis and the prompt employment of less formidable procedures.

On the other hand, Hedblom leaves us a well

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[1] OXYGEN AND CARBON DIOXIDE THERAPY. By Arnold Campbell, M.D., D.Sc. (Edin.), and R. F. Pankhurst, M.C., D.M. (Oxon.), F.R.C.P. (Lond.). Foreword by Sir Leonard Hill, F.R.S. London: Oxford University Press, 1934.

[2] APPARATUS AND TECHNIQUES FOR ROENTGENOGRAPHY OF THE CHEST. By Charles Weyl and S. Reid Warren, Jr., Mercy School of Electrical Engineering, University of Pennsylvania, Springfield, Illinois, and Baltimore, Maryland. Charles C. Thomas, 1934.

[3] INJURIES AND THEIR TREATMENT. By W. Eldon Tucker, M.A., B.Ch. (Cantab.), F.R.C.S. (Eng.). New York: Oxford University Press, 1935.

[4] CLINICAL TUBERCULOSIS. Edited by Benjamin Goldberg, M.D., F.A.C.P., F.A.P.H.A. Vols. I and II. Philadelphia: F. A. Davis Co., 1935.

balanced surgical viewpoint with due recognition of the value of phrenic surgery and pneumothorax

There is necessarily much repetition and also contradiction in not a few instances The latter is rather an asset for it presents the views of more than one author and leaves questions open for discussion One cannot help but be impressed by the practical application of the writings of these thirty-four collaborators It is perfectly evident that they are thoroughly familiar with the everyday problems presented to medical men specializing in this field of medicine

The two volumes are well illustrated with over 640 halftone and line drawings and 9 full-page color plates

While there is much that is superfluous and some unevenness in the quality of the work, still the chapters are all uniformly good and one can absorb useful bits of information from each and every chapter The work is well organized and complete and correlates our knowledge of tuberculosis up to the present moment These two volumes should be of interest to all students of medicine but particularly will they be of value to those specializing in tuberculosis

The editor and his contributors should be highly complimented on their excellent and very thorough presentation and their work should take a high place in our literature dealing with tuberculosis

JOHN W TOWEY

A GREATLY neglected subject has been excellently dealt with by Jameson in his monograph *Gynecological and Obstetrical Tuberculosis*[1] Written as it is, by one who is well qualified both from the viewpoint of the phthisiologist and the gynecologist it fills a definite void in modern gynecological literature The author has gathered together the complete literature on the subject and, in addition, has added his own studies, which were carried out at Saranac Lake, as well as his experiences in the autopsy room and at the bedside in the various sanatoria of this region This material he has correlated from all of the various angles of the subject into a most comprehensive and readable work. For the first time, the modern knowledge of the physiology, diagnosis, and treatment of tuberculosis of the pelvic organs and the ever present problem of tuberculosis and pregnancy are adequately handled in one monograph The book is most highly recommended.

RALPH A REIS

IN *The Principles and Practice of Surgical Nursing*[2] an effort is made by the author to present the nurse with a working knowledge of the diseases that the surgeon meets most frequently It is believed that by obtaining this information the nurse will become a better assistant to the surgeon and not one who merely follows instructions The nurse is expected to be on the lookout for unusual signs and symptoms, to observe the effect of drugs and procedures, and to use her own initiative in the event of a crisis

There are chapters on inflammation, wounds, burns, ulcers and gangrene, tumors, anesthesia, and pre-operative and postoperative care of surgical patients

Surgery of the various regions of the body is discussed as are fractures, diseases of the bones and joints, deformities, and the application of physical therapy to surgery A brief description of the principles of nursing that may be of particular interest in handling each type of surgery, is given, but the actual technique of nursing and nursing procedure are not included in the book.

This work is an effort to satisfy the authors' belief that nurses in the better schools are as well grounded in the sciences fundamental to medicine as were the medical students of 10 years ago and that the nurses are eager for accurate knowledge pertaining to the field of surgery

The inclusion of diagnostic methods with the technique of operative and manipulative treatment of surgical conditions, the dosage of drugs in many instances and the descriptions of such operations, with drawings, as division of the sensory root of the trifacial nerve, operation for aneurism, radical removal of the breast, and certain minor procedures done by a general practitioner might lead one to question the choice of teaching material for other than medical students G L McWHORTER.

THE second edition of Zondek's valuable and extensive monograph[3] is introduced by a short essay on fallacious methods of hormone research that might well be applied to general scientific medical investigations,—"Verlasst man sich also nur auf die klinische—an Fehlerquellen reiche—Beobachtung, so kann der unkritische spielend Theorien machen und seiner Phantasie weiten Spielraum geben" The material presented is, thus, mainly a record of physiological research An exhaustive review is given of the assay, source, preparation, biological action, occurrence in the male, fate, and hormone interrelations of estrogenic substances The pituitary gonadotropic hormones are then taken up in the same way The interplay of the pituitary and gonad is then thoroughly studied. Clinical determination of folliculin and prolan in the blood and urine is described. Polyhormonal menstrual disorders are discussed The occurrence of pituitary follicle stimulating hormone is given and its excretion in male and female genital malignancy described. The clinical use of estrogenic and pituitary substances is covered Reviews of the hormone diagnosis of pregnancy and Zondek's studies of inter-

[1] GYNECOLOGICAL AND OBSTETRICAL TUBERCULOSIS By Edwin M Jameson, B S , M.D Philadelphia Lea & Febiger 1935

[2] THE PRINCIPLES AND PRACTICE OF SURGICAL NURSING By Charles D Lockwood, A.B., M.D , F.A C.S., and John A. Wolfer, M.D , F.A.C.S In collaboration with Mildred E. Newton, B S R.N 2d rev ed New York The Macmillan Co., 1935

[3] HORMONE DES OVARIUMS UND DES HYPOPHYSENVORDERLAPPENS UNTERSUCHUNGEN ZUR BIOLOGIE UND KLINIK DER WEIBLICHEN GENITAL FUNKTION By Dr Bernhard Zondek. 2d enl. ed. Wien Julius Springer 1935

medin, the hormone of the middle pituitary conclude the work. PAUL STARR.

FRACTURES and dislocations are discussed in detail in Kellogg Speed's[1] *Text Book of Fractures and Dislocations* not only to their mechanism but also as to diagnosis and treatment. Illustrations are shown of modern apparatus and their application.

[1] A TEXT BOOK OF FRACTURES AND DISLOCATIONS CONTAINING THEIR PATHOLOGY, DIAGNOSIS, AND TREATMENT. By Kellogg Speed, S.M., M.D., F.A.C.S. 3d ed. thoroughly rev. Philadelphia: Lea & Febiger, 1935.

Each type of fracture is thoroughly covered as to method of reduction, kind of anesthesia (local or general) and as to open and closed methods of reduction.

It is my opinion that this is the most complete book on fracture that has been written. It is really a postgraduate course in modern diagnosis and treatment of fractures. The book is an encyclopedia on fractures; careful reading to digest each word will enable one to gain full knowledge of the subject.

JAMES J. CALLAHAN.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

OXFORD MEDICAL PUBLICATIONS. The Early Diagnosis of the Acute Abdomen. By Zachary Cope, B.A., M.D., M.S. Lond., F.R.C.S. Eng. 7th ed. New York: Oxford University Press, 1935.

GLANDULAR PHYSIOLOGY AND THERAPY. A Symposium Prepared under the Auspices of the Council on Pharmacy and Chemistry of the American Medical Association, 1935. Chicago: American Medical Association, 1935.

CLITOCYBES OMPHALICALES. By L. Devriese. Paris: G. Doin & Cie, 1936.

LEHRBUCH DER GEBURTSHILFE. By Dr. Rud. Th. v. Jaschke. 4th ed. Berlin: Julius Springer, 1935.

ANNUAL REPORT OF THE SURGEON GENERAL OF THE PUBLIC HEALTH SERVICE OF THE UNITED STATES FOR THE FISCAL YEAR 1935. Washington: United States Government Printing Office, 1935.

DISEASE AND DESTINY. By Ralph H. Major, M.D. Preface by Logan Clendening, M.D. New York and London: D. Appleton Century Co., 1936.

THE ART OF MINISTERING TO THE SICK. By Richard C. Cabot, M.D., and Russell L. Dicks, B.D. New York: The Macmillan Co., 1936.

SOCIAL SECURITY. By Edward H. Ochsner, B.S., M.D., F.A.C.S. Chicago: The Social Security Press, 1936.

THE HUMAN FOOT: ITS EVOLUTION, PHYSIOLOGY AND FUNCTIONAL DISORDERS. By Dudley J. Morton. New York: Columbia University Press, 1936.

CLINICAL MISCELLANY. Volume 2, 1935. The Mary Imogene Bassett Hospital, Cooperstown, New York. Springfield, Ill., and Baltimore, Md.: C. C. Thomas, 1935.

BIBLIOGRAPHY OF BLOOD TRANSFUSION. By Dr. E. Koenig. Reduction by Prof. E. Hesse. Leningrad: *Verlag Gibergnal im Grebow* and the Research Institute of Blood Transfusion in Leningrad, 1935.

CARBON. By Dr. Alfonso Asenjo Gomez. Santiago, Chile, 1935.

LEHRBUCH DER KRIMINALPSYCHOLOGIE. By Dr. Carl Franz. 3d enl. ed. Berlin: Julius Springer, 1936.

OXFORD MEDICAL PUBLICATIONS. The Diagnosis and Treatment of Diseases of the Peripheral Arteries. By Saul S. Samuels, A.M., M.D. New York: Oxford University Press, 1936.

A TEXTBOOK OF STERILIZATION. By Weeden B. Underwood, B.S. in E.E. Erie, Pa.: American Sterilizer Co., 1934.

DIAGNOSTIC ROENTGENOLOGY. Ross Golden, M.D., Editor. New York and Edinburgh: Thomas Nelson & Sons, 1936.

OXFORD MEDICAL PUBLICATIONS. Painful and Dangerous Diseases of the Ear. Text book for Students and General Practitioners. By R. R. Woods, M.B., F.R.C.S.I. London: Oxford University Press, 1936.

STERILIZATION: A HANDBOOK FOR PHYSICIANS, HOSPITAL EXECUTIVES AND NURSES. By Harley T. Wyatt, M.S. 3d ed. rev. Madison, Wisconsin: Scientific Morris Company, 1936.

PATOLOGIA QUIRURGICA. Cranio-Cara Raquis-Cuello. By Dr. Conrado Zuckermann.

LE TRAITEMENT CHIRURGICAL DU GOITRE EXOPHTALMIQUE ET DES GOITRES. THE HYPERTHYROIDIE. By Louis Courty and M. Ansel. Paris: G. Doin et Cie, 1936.

ABORTION: SPONTANEOUS AND INDUCED. MEDICAL AND SOCIAL ASPECTS. By Frederick J. Taussig, M.D., F.A.C.S. Sponsored by The National Committee on Maternal Health, Inc. St. Louis: The C. V. Mosby Co., 1936.

SURGERY, GYNECOLOGY AND OBSTETRICS

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THE VALUE OF RADIATION THERAPY IN THE TREATMENT OF CARCINOMA OF THE BREAST

A CRITICAL ANALYSIS OF PUBLISHED STATISTICS

R G HUTCHISON, M B, F R F P.S G, F R C S E, D M R, GLASGOW, SCOTLAND
Assistant Radiologist, Western Infirmary, Glasgow Late Assistant Director, Holt Radium Institute, Manchester

IN 1878 Billroth's statistics showed 8 cures in 143 cases of mammary carcinoma —5 6 per cent

In 1894 Halstead published a description of a radical amputation of the breast, and in the same year Willy Meyer published independently a similar operation With small modifications the procedure as then described has remained—for four decades—the recognized practice in the treatment of mammary carcinoma

Many analyses of results have been published, some, such as those of Lane-Claypon, being of great scope and detail It is interesting to examine these surgical records as a background against which to consider the results obtained by the use of radiation therapy in various forms, and it is significant to do so broadly in two groups those compiled in the earlier years of the radical operation, and those of later years In both, the advance on Bilbroth's 5 6 per cent is striking Tables IA and IB embody the results of an extensive investigation into British, European, and American literature Different authors employ different methods of grouping their cases The various figures have been recorded in the manner selected by the authors, but an endeavor has been made to clarify the position by a simultaneous arbitrary classification into the three broad groups of early, late, and total or unclassified A column has also been added for that group of cases usually classed as inoperable, but perhaps more usefully referred to for our purpose as very advanced

From the figures tabulated in Table IA it will be seen that in the earlier statistics there is a wide range in the percentage results according to the presence or absence of glandular adenopathy, but that when results are judged on total cases operated on, the average percentage cure is 36 4 at 3 years, and 27 5 at 5 years

In Table IB some later figures are tabulated The statistics scarcely better the earlier figures Taking an average over the combined groups the percentage cure figures are 39 4 and 28 1 at 3 and 5 years, respectively

A significant figure is published by Greenough, who gives 15 per cent as the 5 year cure for cases treated by incomplete operations, while Lane-Claypon records a difference of 14 per cent in the 3 year figures for complete and incomplete operations, in favor of the former

Radiation therapy In considering the place of radiation therapy in carcinoma of the breast, it is important to distinguish between radiation combined with surgery, and radiation alone A large accumulation of figures is available for the combined technique In the case of radiation alone, the statistics are more

scanty but at least sufficient are available to make an interesting survey It has been thought desirable to deal with X rays and with radium separately While the radium figures refer to radium therapy alone, it should however be mentioned that in a few cases the X ray statistics include cases in which radium has been combined with X ray therapy

X ray therapy The application of X rays to malignant disease is a relatively recent development. Although the discovery of the X ray was announced in 1895 and although the new ray was in use in the treatment of mammary carcinoma as early as 1901 little advance was made in deep therapy until in 1914 a new era was introduced by the perfection of the Coolidge tube. Modern deep X ray therapy may be regarded as having its beginnings at that time In spite of great advances, the science is even now in its infancy Techniques are changing from year to year in the light of clinical and laboratory research into the problems of quality intensity time-spacing, and sensitivity Even mechanical development is so rapid that the most modern X-ray installation is quickly out of date. These facts cannot be ignored in a review of the present day results of X ray therapy

X-rays combined with surgery Opinions differ as to the efficacy of surgery plus X ray therapy as a routine procedure A wide review of available statistics would seem to be the only means of arriving at a reasoned conclusion. Such a review is incorporated in Tables IIA and IIB As in Tables IA and IB the information has been culled from Continental and American, as well as from British, sources, and again a uniform arbitrary classification into early late and total cases has been made, while retaining the various groupings selected by the individual authors. No attempt has been made to estimate the relative merits of pre-operative, postoperative, or pre-operative and postoperative X rays.

Table VI shows at a glance the comparison between modern results with and without X-rays.

It is interesting to note that all radiologists do not proceed on the same principles. So eminent an observer as Regaud, for example, is opposed to the combination of X-rays with surgery as a routine He advises the pre-operative use of X rays as a means of rendering an inoperable case amenable to surgery and the reservation of postoperative X-ray therapy for certain areas specifically under suspicion in individual cases, or for actual recurrences. Winta allows a period of 6 or 8 months to elapse after operation before proceeding with X ray therapy unless in the event of earlier development of nodules or gland metastases.

X-ray therapy alone Sources of information are here more limited relatively few clinics practicing the method with sufficient frequency and with sufficient stability of technique to enable reliable pronouncements to be made Nevertheless, it has been found possible to collect some percentage figures from the literature, and these are set forth in Tables IIIA and IIIB The same method of tabulation has been employed as in the previous tables in order that comparable results may be readily visualized.

For convenience again, Table VI has been drawn up to allow of immediate comparison and contrast of the results of surgery surgery plus X rays, and X rays alone, as obtained by modern technique.

Radium therapy The isolation of radium was announced to the Academy of Sciences in Paris in 1898. Its application to therapeutics was suggested in 1901 Before the Great War radium centers were beginning to spring up in this country Already the sensitivity of carcinoma of the breast to the new type of radiation was known, and Finzi, finding difficulty in effecting adequate penetration had visualized its use as an external application when sufficient supplies should become available. Twenty five years ago, Dominici used radium in the axilla as a postoperative measure

The greatest advances have taken place in the last decade, and we are now thanks to the work of Stahel, Sievert Mayneord Parker and many others, in the early years of a new era, in which the amount of energy actually delivered to the tumor and to the tissues will be measured in physical units. The impor

TABLE IA—SURGERY ALONE

Author and published groupings	Year of publication or period of investigation	Percentage cure 3 years or more				Percentage cure 5 years or more			
		Early	Late	Total or unclassified	Very advanced	Early	Late	Total or unclassified	Very advanced
Greenough and Simmons Radical operation cures	1894–1904							21	
Westermark (quoting Brattstrom)	1898–1915							23	
Tixier	1902–1914							38	
Westermark (quoting Brattstrom)	1905–1915							25 5	
Greenough, Simmons and Barney	1907			20 9					
Ochsner	1907			34 7				22 4	
Bloodgood (a) Glands not involved (b) Glands involved (c) Operable, not grouped	1908	85	30	42					
Depage	1908			48					
Greenough and Simmons Radical operation cures	1911–1914							32	
Judd	1912							30	
Lindenberg	1914							28	
Averages		85	30	36 4				27 5	

tance of this development is fundamental Radium therapy is being lifted from the realm of the empirical to the level of an exact physical science A wealth of information is becoming available as to the sensitivity (physically determined) of different tumors, and of the same tumor in varying sites, and rapid advance will be assured by the correlation of the effects produced by the γ-rays of radium on a standardized and international scale

Surgery plus radium From a study of the methods employed in many different clinics, it is apparent that after radium treatment of cancer of the breast, local or radical amputation is frequently carried out, either as a routine procedure or on account of unsatisfactory resolution In some clinics radical operation is followed by the application of surface radium applicators to various areas Wintz carries out a local excision of tumor mass or gland in order to obtain pathological confirmation of the nature of the growth Various combinations of these procedures are carried out by different workers

Table IV furnishes an interesting comment upon this aspect of the problem It incorporates the only available figures bearing directly upon this section Both sets of figures refer to the implantation of radium at the time of operation This method is often criticized on the ground of delayed healing The criticism would appear, however, to be valid only in so far as radium is allowed to come into relationship to devitalized skin flaps After an experience of 98 cases, Trout and Peterson state that there has been no interference with the healing of the wound

Radium alone Various combinations of surface and interstitial radium therapy have been used, and have been examined critically by the writer elsewhere [1] The available figures are few in number, but tabulation has been resorted to as being the only means of giving a bird's-eye view of the present position, and of offering a ready comparison with the data already submitted for the other groupings The results will be found collected in Table V Radium therapy can hardly be regarded as having passed beyond its early stages, and no attempt has been made to differentiate between earlier and later techniques The averages of Table V have nevertheless been included in Table VI so that they may be referred to easily

[1] Brit. J Surg., 1935 22 465–474.

TABLE IB—SURGERY ALONE

Author and published groupings	Year of publication or period of investigation	Percentage cure 5 years or more				Percentage cure 5 years or more			
		Early	Late	Total or weighted	Very advanced	Early	Late	Total or weighted	Very advanced
Trout and Petersen	[illegible]								
Martzington	[illegible]								
a. No glands	[illegible]	[illegible]				[illegible]			
b. Glands involved			[illegible]				[illegible]		
No glands	[illegible]	[illegible]				[illegible]			
b. Glands involved			[illegible]				[illegible]		
Perthes	[illegible]			[illegible]				[illegible]	
Greenough and Jamieson	[illegible]								
a. No glands						[illegible]			
b. Glands slightly enlarged							[illegible]		
Glands markedly enlarged							[illegible]		
(average cases)									
Kostrzeb	[illegible]								
a. With glands		[illegible]	[illegible]			[illegible]	[illegible]		
b. Without glands									
c. Total cases				[illegible]				[illegible]	
Wilmanns	[illegible]								
a. All cases		[illegible]		[illegible]					
b. Group			[illegible]						
Group									
d. Group 3					[illegible]				
Rosser	[illegible]			[illegible]				[illegible]	
Gage and Adams	[illegible]			[illegible]					
Peck and White	[illegible]					[illegible]			
a. Without auxiliary metastases							[illegible]		
b. With auxiliary metastases									
Total								[illegible]	
Haggard and Dougherty	[illegible]							[illegible]	
Wahlen	[illegible]			[illegible]					
Lane-Claypon	[illegible]								
a. Class		[illegible]							
b. Class			[illegible]						
Class 3									
d. Total with "complete" operations				[illegible]					
Lee and Cornell	[illegible]							[illegible]	
Lehmann	[illegible]			[illegible]				[illegible]	
Heidenhain	[illegible]			[illegible]				[illegible]	
Amreinetz and Hofmeister	[illegible]								
Group		[illegible]				[illegible]			
Groups m and rb			[illegible]				[illegible]		
Group rc			[illegible]						
Group 3					[illegible]				[illegible]
Total				[illegible]				[illegible]	
Bruns and Matzen	[illegible]			[illegible]				[illegible]	
Dahl-Iversen	[illegible]			[illegible]					
Meyer	[illegible]								
Schmitz and Orbach	[illegible]			[illegible]				[illegible]	
Rochlin	[illegible]			[illegible]				[illegible]	
Dieckhoff	[illegible]			[illegible]				[illegible]	
Hagemann	[illegible]								
a. Glands not involved		[illegible]				[illegible]			
b. Glands involved			[illegible]				[illegible]		
Lane-Claypon	[illegible]								
Class		[illegible]				[illegible]			
Class			[illegible]				[illegible]		
Class 3			[illegible]						
Freemann	[illegible]			[illegible]				[illegible]	

TABLE 1B—SURGERY ALONE—Continued

Author and published groupings	Year of publication or period of investigation	Percentage cure 3 years or more				Percentage cure 5 years or more			
		Early	Late	Total or unclassified	Very advanced	Early	Late	Total or unclassified	Very advanced
Greenough	1929							34	
Pfahler and Widmann	1929			32				31 3	
Schmitze. Group 1	1929					69 2			
Handley	1930			47					
Himmelmann and Lehmann. a. Steinthal 1 b Steinthal 2 c. Steinthal 3 d Total	1930	73 5	34 7	42 5	7 1	66 6	25	34 6	7 7
Pfahler and Parry a. Glands not involved b Glands involved	1930	75	30			77	20		
Westermark, quoting for a Dahlgren b Neander c Mystrom	1930							15 16 8 21 5	
Keynes	1930–1931			45 2				37	
Gobell and Magens Group 1 Group 2 Group 3 Group 4 Total	1931	100	67 4 42 8	60 1	25	100	53 5 28	46 6	8 3
Hintze	1931							28 4	
Stubenbord	1931							9	
Wintz a Steinthal 1 b Steinthal 2 c. Steinthal 3	1931	75	28		7				
Adair	1932							10	
Danis	1932			59				51	
Hintz	1932							34	
Klingenstein a. Without glands b With glands c. Total	1932					40	17	23	
Mathews No axillary involvement	1932					64 4			
Pfahler a. Without glands b With glands	1932	75	32			80	24 5		
Taylor a Without axillary involvement b All radical operations	1932					70		30	
Gask	1933							36	
Pearce Gould a Stage 1—no glands b Stage 2—glands c All cases	1933	65 9	39 4	48 3		57 4	22 1	33 1	
Averages		77 9	36 0	39 4	14 2	71 3	25 0	28 1	9 5

TABLE IIA.—SURGERY PLUS X RAYS

Author and published groupings	Year of publication or period of investigation	Percentage cures 5 years or more				Percentage cures 5 years or more			
		Early	Late	Total or weighted average	Very advanced	Early	Late	Total or weighted average	Very advanced
Fletcher and Perry a. Pre- and postoperative X-rays All classes b. Postoperative, no glands Postoperative with glands d. Postoperative, all classes	[illegible]	[illegible]	63	55 [illegible]		84	73	67 [illegible]	
Schwarz a. Group b. Group	[illegible]					[illegible]	16		
Harrington a. Without glands b. With glands	[illegible]	[illegible]	41 3			[illegible]	[illegible]		
Perkins Group	[illegible]	84							
Walther	[illegible]			37					
Greenough	[illegible]							34	
Lehmann Old technique	[illegible]			33				30	
Schmitz a. Groups and b. Group c. Group 3						84 3	47	71	
Averages		87 3	51 8	64 3		[illegible]	33 6	41	

TABLE IIB.—SURGERY PLUS X-RAYS

Author and published groupings	Year of publication or period of investigation	Percentage cures 5 years or more				Percentage cures 5 years or more			
		Early	Late	Total or weighted average	Very advanced	Early	Late	Total or weighted average	Very advanced
Fletcher and Perry a. Pre- and postoperative All classes b. Postoperative—no glands Postoperative with glands d. Postoperative—all classes	[illegible]	95	64	64 3		93	57	34 73	
Amreinetz and Hellmann Group a. Groups 1a and 1b c. Group 2a d. Group 3 Total	[illegible]	100	[illegible] 7 [illegible]	86	57	100	[illegible] 3 [illegible]	44 4	9 3
Breuer and Mayer	[illegible]			66				39	
Meyer	[illegible]							3 3	
Schmitz and Orbeck	[illegible]			37				44 4	
Rochelle	[illegible]			34				43	
Lee a. Pre- and postoperative irradiation b. Postoperative irradiation	[illegible]							[illegible] 35	
Harrington a. Without glands b. With glands	[illegible]	86 7	43 1			64	36 3		
Fletcher and Widmann	[illegible]			38 3				43	
Schmitz a. Group b. Group 1	[illegible]						1 7		1

TABLE IIB—SURGERY PLUS X-RAYS—Continued

Author and published groupings	Year of publication or period of investigation	Percentage cure 3 years or more				Percentage cure 5 years or more			
		Early	Late	Total or unclassified	Very advanced	Early	Late	Total or unclassified	Very advanced
Evans and Leucutia	1930								
a Without glands		76 5				70 6			
b With glands			62 2				46 7		
Himmelmann and Lehmann	1930								
a Steinthal 1		100				50			
b Steinthal 2			25 9				18 2		
c. Steinthal 3					28 6				
d Total				32 4				16 7	
Pfahler and Parry	1930			45 5				35	
Trout and Peterson	1930							55	
Westermark	1930								
a Quoting Dahlgren								29 3	
b Quoting Brattstrom								40	
c. Diathermy plus irradiation								28 6	
d Postoperative irradiation									
Steinthal 1						60			
Steinthal 2							29 1		
Steinthal 3									0
e. Pre and postoperative irradiation									
Steinthal 1						75			
Steinthal 2							35 5		
Steinthal 3									16 7
f Electro-endothermy plus irradiation									
Steinthal 1						100			
Steinthal 2							42 9		
Steinthal 3									15 4
de Backer	1931			50					
Billich	1931			58 4				39 6	
Gobel and Magens	1931								
a Group 1		100				100			
b Group 2			64 8				52 1		
c Group 3			41 7				33 3		
d Group 4					0				0
e. Total				57 7				47 7	
Hintze	1931							37 9	
Lee	1931								
a. Grade A						45			
b Grade B							24		
c. Grade C									13
Wasslink	1931								
a Without metastases		93 3							
b With central axillary glands			65 2						
c. With peripheral axillary glands			14 8						
d With metastases above axilla					9 5				
Adair	1932							38 2	
Hintze	1932							53	
Pfahler	1932								
a. Pre and postoperative X ray									
1 Without glands		65				58			
2 With glands			62				57		
b Postoperative X ray									
1 Without glands		66				87			
2 With glands			64				58		
c. Averaging various authors									
1 Without glands		92				74			
2 With glands			50				37		
Portmann	1932								
a Group 1						65 6			
b Group 2							56 3		
c Group 3									6 2
d. All cases								42 [illegible]	
Webster	1932								
Stages 2 and 3				47				42	
Averages		89 9	51 0	55 7	16 3	74 7	41 0	40 9	9 1

TABLE IIIA—X-RAYS ALONE

Author and published percentages	Year of publication of period of observation	Percentage over 3 years or more				Percentage over 5 years or more			
		Early	Late	Total or nearly total	Very advanced	Early	Late	Total or nearly total	Very advanced
Plaikey and Perry Primary operable b Primary inoperable	[illegible]	[illegible]			[illegible]	[illegible]			[illegible]
Schwartz Grade b Grade	[illegible]					[illegible]			
Wintz Stenthal b Stenthal Stenthal 3 d Total	[illegible]	[illegible]	[illegible]	[illegible]					
Averages		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		[illegible]

EVALUATION

Examination of the various figures in the foregoing tables leads to some interesting conclusions. In the first place, it is apparent that surgery *per se* is no longer unchallenged as the treatment of choice in mammary carcinoma, even in early cases without glandular adenopathy. Minor improvements in operative technique may yet take place but broadly speaking it would appear that the resources of surgery have been exploited to their limit. That this is so is borne out by the *very slight improvement in the surgical results* during the last 20 years or so.

Much discussion has taken place in recent times regarding the desirability of combining surgery with radiation. Study of the figures obtained in the course of this investigation allows of only one conclusion, namely that the combination of X rays with surgery offers a better chance of cure than does surgery alone. In the early cases, the advantage of this technique is not striking but in the later cases, and when total cases are considered the improvement in the results is seen to amount to about 20 per cent at the 3 year period and 15 per cent at the 5 year period, an advance so great that it cannot reasonably be attributed to chance. It will be noted, and perhaps at first sight with surprise that the very advanced cases do not appear to reap any advantage from the combined technique. To the writer it seems that the explanation lies in the damage done by encroachment with the knife upon malignant tissues.

The steady improvement in X-ray technique has been mentioned already and is manifest in Tables IIIA and IIIB which show the results of X ray therapy alone. Here improvements of later upon earlier results are seen to be of the order of 40 per cent at 3 years and 20 per cent at 5 years. The 3 year figure of 94 per cent for early cases is remarkable. Wintz has stated that in the Steinthal group I it is *not possible to improve* upon the results of surgery but that in Steinthal groups II and III X radiation *per se surpasses the best results of operation*. But while the figures for X radiation alone are few compared with those for surgery or for the combined technique, it must be conceded that in the hands of the expert, when the technique has been evolved from large experience and is applied in a scientific manner the results of radiation alone are seen to equal or surpass those of any other method, even in the early cases. It is impossible, however to emphasize too strongly that such radiation results are obtained only when scientific methods prevail, and not by the random application of X-rays of unknown quality and intensity and in *unknown amount*.

Not least striking are the results in the very advanced cases, and it is seen that in this sphere radiation alone improves, *not only* upon surgery but also upon surgery plus X rays. This fact would appear to offer an interesting commentary upon the *danger of transgressing surgically upon malignant tissues*. Tissues traumatised by operative surgery

TABLE IIIB—X-RAYS ALONE

Author and published groupings	Year of publication or period of investigation	Percentage cure 3 years or more				Percentage cure 5 years or more			
		Early	Late	Total or unclassified	Very advanced	Early	Late	Total or unclassified	Very advanced
Pfahler and Parry a. Primary operable b Primary inoperable	1922–1927	93			48	80			32
Wintz a Grade 1 b Grade 2 c. Grades 1 and 2	1925	95 2	68 2					48 5	
Wintz	1926				18 1				18 8
Lee a. X-rays b X rays and radium	1928							11 37	
Webster a. Stage 1 b Stages 1 and 2	1928	100		75					
Jungling	1929				11 1				
Pfahler and Widmann a Operable b Inoperable	1929			83 3	47			50	23 4
Schmitze Group 4	1929								3 2
Lee Grade A	1931					55			
Wintz a. Steinthal 1 b Steinthal 2 c. Steinthal 1 and 2 d. Steinthal 3	1931	96	70	77 3	21	76	46 5	55 4	10
Adair	1932							24 2	
Hintze	1932								6 1
Pfahler a. Grade 1 b Inoperable {1 {2	1932	88			35 39	82			25 30
Webster Operable and borderline	1932							70	
Averages		94 4	69 1	78 5	31 3	73 3	46 5	42 3	18 6

are unable to tolerate a dose of radiation as large as can be applied to undamaged tissues and therefore the risk is real that when malignant tissues are opened up by the knife it may no longer be possible to deliver a lethal dose of X-ray therapy to any residue of malignant tissue The same consideration undoubtedly arises also in relation to surgery plus radium

Radium therapy alone presents an encouraging record, and further improvements are to be looked for as technical difficulties are overcome At the present time, however, it does not quite produce the results achieved by other methods Figures for radium beam therapy in relation to breast cancer do not appear to be available as yet, and expression of any opinion upon this matter would be premature

Statistics are scanty regarding radium combined with surgery There is no justification for suggesting that this is the ideal method for dealing with carcinoma of the breast Nevertheless the results of Handley and of Trout and Peterson are interesting, as being a practical justification of a logical procedure In the writer's opinion, however, none of the methods usually employed explores the full possibilities of the combination Such a technique should achieve its maximum benefit in those cases which are surgically operable The average percentage of 5 year surgical

TABLE IV—SURGERY PLUS RADIUM

	Author	Year of publication	Percentage cure 3 years	Percentage cure 5 years
Surgery alone	Handley	[illegible]	47	
	Trout and Peterson	[illegible]		11
Surgery plus radium	Handley	[illegible]	56 3	
	Trout and Peterson	[illegible]		[illegible]

TABLE V—RADIUM ALONE

Author and published percentage	Year of publication or period of human cases	Percentage cure 3 years or more				Percentage cure 5 years or more			
		Early	Late	Total or unclassified	Very advanced	Early	Late	Total or unclassified	Very advanced
Kronig (Quoted by Schmitz) Group 1 Group 2 Group 3	[illegible]					11 4	16 4		
Wharton Operable and inoperable	[illegible]					60			
Kerwin Class 1 Class 2 Class 3	[illegible]	77 7	36 3 36						
Kerwin Operable Inoperable	[illegible]					60			28
Ravin and Hare (Nat Radium Comm Report) Stage 1 Stage 2 Stage 3	[illegible]	64	39 9 34 9						
Averages		70 9	36 6			47	36 4		19 3

TABLE VI—COMPARATIVE AVERAGES

	Percentage cure 3 years or more				Percentage cure 5 years or more			
	Early	Late	Total or unclassified	Very advanced	Early	Late	Total or unclassified	Very advanced
Surgery alone	77	36	39	11	77 1	31	26	9 1
Surgery plus X rays	60	37	34 7	36 3	7 7	43	40	4
Radium alone	70 9	36 6			47	36 4		19 3
Values above	64	60	36 3	3	3	36	41 3	12 6

Note also Surgery plus radium (two authors only)
Percentage cure 3 years—36 1
Percentage cure 5 years—30

cures has been shown to be just under 30 A proportion of the remaining 70 per cent is lost on account of unsuspected or invisible deposits beyond the limits of surgical dissection It is this proportion which ought to be saved in part by the utilization of the surgical access for the introduction of radium into the areas in question In other words, radium should be used to extend the scope of the radical operation, and not in the hope of compensating the deficiencies of surgical procedures otherwise faulty

It is evident that, when confronted with a case of cancer of the breast a considerable array of possible lines of attack lies before the medical man, and it is not surprising that he should feel at times a considerable weight of responsibility in selecting that which will most fully serve the best interests of his patient The work embodied in the foregoing pages has involved careful sifting of a large mass of literature pertaining to this problem and it is hoped that it will serve a useful purpose in lessening the burden of the choice by presenting some concrete facts material to the decision In addition, the writer hopes that the findings may be of some scientific importance at an interesting period in the history of radiation therapy

SUMMARY

The author presents a statistical survey of British, European, and American literature, dealing with the treatment of mammary carcinoma The numerous published classifications have been arbitrarily arranged for comparison into early, late, total and very advanced From a study of the literature and of the figures obtained the following conclusions are reached

1 Surgery is no longer unchallenged as the treatment of choice

2 Radiation combined with surgery produces results better than those of surgery alone

3 X-ray therapy, when scientifically employed, has been shown to produce results which surpass those of any other procedure

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THE HEALING PROCESS IN TUBERCULOUS SPONDYLITIS

A Histopathological Case Study

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INTRODUCTION

A CASE of extensive tuberculosis of the spine, which healed under conservative treatment only, provided material for instructive pathological studies Destructive bone changes combined with osteoporosis, so common in the active stages of tuberculosis, are absent here In this case, which was of many years' duration, the bone tissue went on to healing, so that osteosclerosis developed at the sites of skeletal lesion, in one place complete union by bony fusion occurred between two vertebræ In an era when surgery in tuberculosis is on the rise, knowledge of two factors may be of value first, healing may occur without surgical intervention, second, in cases of bone infection, sclerosis as seen in the roentgenogram does not necessarily mean the healing of a simple osteomyelitis, but may indicate the healing of an old tuberculous lesion

The tuberculous disease of the spine in this study had been existent in a quiescent stage, for many years No signs of activity were evident even at the time of death, which resulted from a marked exacerbation of pulmonary disease and a miliary dissemination of the tuberculosis shortly before the end Healing was indicated by many tissue changes, such as fibrosis of bone marrow, osteosclerosis, bony fusion, sequestration of necrotic bone, organization of tuberculous abscesses, and scarring of diseased intervertebral discs

Furthermore, healing was associated with evidence of immunity of bone tissue to tuberculosis, a fact substantiated by histopathological findings Bone tuberculosis and immunity in tuberculosis have been studied extensively, yet very little information is available which correlates these investigations and develops the idea of bone immunity to tuberculosis Randerath quotes Askanazy in regard to fibrosis of bone marrow in tuberculosis and presents his own material, but his descriptions are too morphological In this article the pathological findings are interpreted in the light of the biological and immunological processes

In addition, several interesting observations were made in the routine microscopical examinations of sections representing the eight vertebral segments which were involved in this case These findings are included in this report under the separate heading of special studies

CLINICAL DATA[1]

On examination of the patient when he was 32 years of age, a diagnosis of pleurisy with effusion and right lumbar gravitational abscess was made During the next 3 years other abscesses formed about the right hip and sacral region, as well as in the dorsolumbar region, where a kyphoscoliosis had developed with a gibbosity at the eleventh and twelfth dorsal vertebræ Drainage of abscesses and dietary regimen resulted in such marked improvement that the patient was sent home (about 6 years after time of first examination) He returned 1½ years later with marked aggravation of the pulmonary symptoms Several days later his temperature rose to 102 2 degrees Fahrenheit and he developed opisthotonus, a positive Kernig's sign, and cramps in the right arm Six days after the last admittance he became comatose and died

The autopsy findings showed chronic pulmonary tuberculosis with advanced involvement of all lobes There were tuberculous ulcers of the trachea, larynx, hypopharynx, and epiglottis Solitary ulcers were found in the large bowel and lower ileum and miliary tubercles in the kidneys, spleen, and liver The right heart was hypertrophied. The meninges were found to be free

Examination of the spine revealed Pott's disease extending from the eighth dorsal to the third lumbar vertebra, healing had occurred with eburnation and gibbus formation at the dorsolumbar junction, where the first lumbar vertebra was reduced to a wedge-shaped fragment A small sequestrum was present in front of this segment, while above it the intervertebral disc was completely destroyed The eleventh and twelfth dorsal vertebræ were fused to each other by bony union At this level abscesses

[1] I am indebted to Dr Ernst Freund, Department of Orthopedic Surgery, Children s Hospital for help in preparing this paper and for the use of pathological material from his private collection. Since submitting this manuscript Dr Freund has become associated with the Florida Medical Center, Venice Florida.

occurred, both in front and behind elevating the anterior and posterior longitudinal ligaments, respectively from the surfaces of the vertebral bodies A right paravertebral abscess communicated with the prevertebral and postvertebral abscesses, which may have furnished the avenue by which infection traveled up and down the spine, involving the other segments. Many sinuses, which were partially obliterated, were noted over the lumbar spine and over the sacrum

The rather constant narrowing of the intervertebral spaces gave evidence of the involvement of the intervertebral discs by early contact with tuberculous pus The reaction of the bone tissue which was in relation to the infection at the surfaces was manifested by sclerosis of the bony trabeculae associated with fibrosis of the bone marrow In other places, which in most instances were more distant to the infective foci, the bone marrow was myelogenous in character and was associated with porotic bony trabeculae (Fig 6)

MICROSCOPICAL STUDIES

The accompanying X-ray photograph (Fig 1) of the anatomical specimen reveals the general configuration and grosser bony changes of the diseased portion of the spine. A complete, detailed study was made of each of the eight vertebral segments, but only a representative composite picture of the material is presented herewith.

Bony trabecule The structural transformation in the bony trabecule is secondary to changes in the bone marrow where it has reacted to the diffusion of tuberculous toxins. The existence of these toxins is inferred from the presence of prevertebral, postvertebral, and intervertebral abscesses (Fig. 2 C) The bone marrow close to the abscess formation where the concentration of toxins is greatest, shows healing by fibrosis. The bony trabecule in these areas have healed by osteosclerosis This picture is strikingly different from that seen in active tuberculosis when osteoporosis and bone destruction are prevalent The bony trabecule which are quite thick and dense in most places owe their size to marked bone apposition as shown by the presence of many dark blue cement and apposition lines (Fig 3) Whereas the cement lines may be quite irregular often lacunar in outline, the apposition lines usually run parallel to the surface of the bony trabecule indicating different periods of apposition. The trabecular surface, which is smooth in most places, may be covered by a blue line of quiescence. In this stage there is neither bone apposition nor bone resorption actually taking place. However as soon as apposition by osteoblasts again becomes active the blue line on the surface becomes included in the trabecula It is now an apposition line. These blue lines are of great aid in retracing the development of the pathological bone tissue, and make possible a clearer understanding of the entire pathological process.

The picture of osteosclerosis, as here presented is a common one in regions of mechanical static stresses, where bone tissue becomes re-enforced by bone apposition under a stimulus such as weight-bearing, for example In this case, however the mechanical static demands are insignificant and may be ignored By way of illustration the bony trabecule in the region of the prevertebral abscess show osteosclerosis and the marrow spaces are filled with fibrous bone marrow In a segment only a few millimeters above however the bony structure (where it forms one wall of the prevertebral abscess) shows marked osteoporosis. Mechanical irritation certainly cannot account for the sharp division between advanced osteosclerosis in one vertebra with the marked osteoporosis in the segment so close by This osteosclerosis, which, therefore, must be inflammatory in nature is similar to that seen in cases of healing simple osteomyelitis. This point is interesting because it demonstrates that a very high degree of osteosclerosis may also occur in a tuberculous lesion when the bone marrow is stimulated to fibrosis and osteogenesis by a relatively avirulent toxin or when the marrow develops an increased resistance to the toxin Farther away from the intervertebral space and its abscess, the bony trabecule become thinner and fewer in number Their structure, nevertheless, is entirely pathological in that they still show many cement and apposition lines. However the cement lines frequently show lacunar outline, which means that the vertebral bone tissue has undergone considerable structural transformation even at some distance from the focus of infection

The foregoing picture makes it evident that the osteosclerosis has developed by a gradual,

prolonged process of bone transformation In the early stages lacunar resorption of the bone tissue lead to marked osteoporosis, due partly to disuse and partly to inflammation in the areas of tuberculous lesions As the activity of the disease subsided, new bone became apposed on the lacunar surfaces of the old porotic trabeculæ, resulting in the picture of osteosclerosis described previously

Markedly active bone resorption is relatively rare in this case and occurs only in a few areas in which the tuberculous process is still active So, for example, the lacunar type of bone resorption is seen along the ends of the bony trabeculæ which point toward the intervertebral space, many osteoclasts can be seen here in Howship's lacunæ A similar picture is seen where the trabeculæ are in relation to abscesses filling in the intervertebral space The peripheral fibrous tissue wall, derived from granulation tissue, causes irregularity of the bone tissue This active bone resorption is partly due to mechanical irritation, especially pressure, exercised on the superficial bony trabeculæ, in greater part, it results from the irritation caused by toxic and inflammatory agents in the intervertebral pus cavity

However, as obliteration of the abscess cavity occurs, the underlying bone tissue escapes pressure and new bone becomes apposed This is nicely illustrated close to the patent prevertebral abscess, where the bony trabeculæ show signs of osteoclasia However, when secondary obliteration of the abscess cavity has occurred by reattachment of the anterior longitudinal ligament to the bone surface, such signs of osteoclasia are absent On the contrary, apposition of primitive bone tissue has taken place in thin layers, separated from each other by thin blue apposition lines This clearly indicates that bone resorption occurred as a result of the open prevertebral abscess In addition to the osteoclasia of bone, aforementioned, in relation to a focus of destruction, numerous areas of osteoporosis and bone resorption are seen within the vertebral bodies at some distance from a site of inflammation The reason for the presence of these isolated areas of osteoporosis in such close proximity to areas of sclerosis (Fig 4, *D*, *E*) is revealed by a closer study of the changes which had taken place in the bone marrow

Bone marrow In areas showing marked osteosclerosis of the trabeculæ, the bone marrow, almost without exception, is fibrous This is especially true close to the intervertebral space, where hyperemic, loose, fibrous bone marrow is found quite densely infiltrated by lymphocytes The degree of sclerosis is apparently in direct proportion to the fibrosis of the bone marrow A somewhat similar picture of bone marrow fibrosis is seen in cases of fracture followed by pseudarthrosis, in which fibrosis develops to a limited extent to either side of the fracture space by mechanical static irritation However, in this case inflammation and not mechanical stress is the cause of fibrosis The presence of isolated areas of hematopoietic bone marrow (as already noted) in the midst of a prevailing fibrosis of bone marrow supports the inflammatory theory

As the distance from the destroyed intervertebral space increases, the fat cells in the fibrous bone marrow become more numerous, especially along the endosteal surfaces of the bony trabeculæ All these fat cells are in a very advanced stage of atrophy and show the characteristic halo of edema The fat cell itself is very small, usually reduced to the signet ring form After disappearance of its fat content, the cell protoplasm may stain dark red, the nucleus is found centrally or peripherally This is a common picture of simple atrophy of fatty bone marrow In this case it is complicated by the disappearance of the hematopoietic elements and the presence of considerable fibrin This picture represents a transitional stage between the fibrous bone marrow close to the intervertebral space and the myelogenous bone marrow in the remote corners of the vertebral body (Fig 4, *C*)

The method of transition can be followed histologically at the periphery of the area of fibrous bone marrow In the first stage, a very marked hyperemia exists, so that the entire capillary network of the bone marrow is heavily filled with blood Next, a very rapid disappearance of the hematopoietic elements of the bone marrow ensues, resulting from the strong

deleterious effect of the toxins on the specific bone marrow cells. As the specific elements fade the fatty bone marrow cells, which are normally more or less hidden by the myelogenous tissue, come into sudden prominence (Fig. 5 *B*) Although the fat cells seem to resist the infection better than the specific elements, they ultimately undergo atrophic changes with the characteristic halo of edema (Fig. 5, *C*)

This atrophy of the fat cells must be considered as a result of toxic damage and not as a simple marantic atrophy due to the general cachexia of the patient. If cachexia were the basis for the atrophy all fat cells would be expected to suffer equally However the fat cells in the areas of hematopoietic bone marrow are found to be perfectly normal in size and show no halos of edema. Consequently the local toxic damaging substances, and not the patient's constitutional debility must be blamed for the fat cell atrophy In the final stage which follows soon fibrosis develops and collagenous fibers spread between the fat cells, giving the characteristic picture of *Gerustmark*, which gradually but progressively changes into fibrous bone marrow

To recapitulate The bone marrow reacts to the stimulation of tuberculous toxins in direct proportion to their concentration Close to the focus of bone destruction, where the concentration of toxins is greatest the bone marrow responds by marked fibrosis and osteogenesis. The toxins become more dilute as they diffuse into the bone tissue for some distance and the bone marrow reaction is less marked atrophic fatty bone marrow with moderate fibrosis and osteosclerosis results. In the parts farthest removed from the focus of toxin production the damaging substances are most dilute or entirely absent here normal hematopoietic bone marrow still persists and the bony trabeculae are thin and porotic In brief, the degree of fibrosis of the bone marrow is the index of the extent and intensity with which the toxins have invaded the bone tissues (Fig 8)

Refutation of pyogenic cause of osteosclerosis The objection may be raised not unreasonably that factors other than tuberculosis may be responsible for the development of osteosclerosis. The mechanical factor has already been discussed there still remains the consideration of pyogenic infection, in the sense of the simple form of osteomyelitis, as a basis of osteogenesis.

Any case of tuberculosis with an open sinus is likely to become superinfected from without, and impose a secondary non-specific osteomyelitis upon a tuberculous lesion. Theoretically a hematogenous infection of a tuberculous abscess is also possible By way of illustration, the fused eleventh and twelfth dorsal vertebrae show marked osteosclerosis and bony union (Figs. 1 and 11) which could be considered as the result of an osteomyelitic process rather than a tuberculous one The considerable osteosclerosis and bone marrow fibrosis, which is so commonly found in healing osteomyelitis, is also found here and in this manner favors the diagnosis of simple osteomyelitis.

However in none of the tissues examined was an active pyogenic infection suggested by signs of acute inflammation and pus cells Even the abscess cavities present are filled with exudate typical of tuberculous pus Tubercles are present in the abscess wall, but they are rather few in number Furthermore, as Erdheim has shown, uncomplicated tuberculous osteitis is capable of producing marked osteosclerosis Erdheim introduced the term "para-tuberculous osteosclerosis" for this entity which he studied in the skull bone, and which is especially well illustrated in cases of tuberculous osteitis of the os calcis without sinus or abscess formation. This evidence substantially supports the view that fibrosis and osteosclerosis in this case are due to tuberculosis and not to pyogenic infection.

BONE IMMUNITY

Miliary tubercles Bone tuberculosis in the healing stage, as studied in this case furnishes histopathological evidence that bone tissue may acquire immunity to tuberculosis Microscopically the preparations reveal a great number of young miliary tubercles, consisting of a few epithelioid cells, but without any giant cells or lymphocytes These tubercles represent a recent dissemination and correspond clinically to the terminal infection

which probably originated from the active pulmonary lesions and had no direct relation to the old tuberculous process in the spine Most of the young tubercles occur quite constantly in areas where normal or almost normal hematopoietic bone marrow still exists Practically none can be seen in regions of fibrous bone marrow Those tubercles which do appear in fibrous marrow show a tendency to conglomeration and apparently are of older age than the tubercles of the terminal shower

The conglomerate tubercles are found anteriorly in the superficial marrow spaces which communicate with the abscess cavity Except for these areas the fibrous bone marrow is free from active signs of tuberculosis Conversely, the marrow spaces filled with hematopoietic bone marrow show a relatively frequent incidence of miliary tubercles, so that five or six tubercles in a low power field are not uncommon (Fig 6)

The predilection of the miliary tubercles to the myelogenous marrow and their absence from fibrous marrow indicates a difference in the allergy of these two tissues (Fig 7) The fibrous bone marrow apparently has developed a higher resistance to the tubercle bacillus than the hematopoietic marrow This resistance is undoubtedly acquired by the bone marrow which has been inoculated for a long period of time by the toxins diffusing from the foci of active tuberculosis Although bone ranks high among the tissues predisposed to infection by the tubercle bacillus it apparently can develop a high degree of immunity to such infection if exposed to the toxins for some time

However, it should be noted that trauma may weaken the allergic resistance of fibrous tissue This factor is brought out in the region of the wedge-shaped first lumbar vertebra Its eroded upper surface, exposed to the abscess cavity, shows a progressive tuberculous lesion with a relatively great number of tubercles This can be explained by the traumatization which the fibrous bone marrow suffers as soon as it becomes denuded of protective bony layers The trauma reduces the allergic resistance of this tissue and may abolish it entirely

Fig 1 Roentgenogram of the involved segments of the spine from the eighth dorsal vertebra above to the third lumbar vertebra below There is complete bony ankylosis between the eleventh and twelfth dorsal vertebræ The first lumbar vertebra is reduced to a wedge shaped fragment

Origin of toxins The origin of the toxins—capable of stimulating bone marrow to fibrosis, osteogenesis, and immunity—is still open to conjecture Three sources are possible· first, pyogenic superinfection, second disintegration of diseased tissues, and third a tuberculous toxin The reasons for eliminating superinfection of a tuberculous lesion by a pyogenic organism have already been discussed

Next, the origin of toxins due to destruction of tissues comes under consideration The decay of tissues involved by an active tuberculous lesion may lead to the formation of toxins By diffusion they invade and irritate the bone marrow of the surrounding tissues which are not directly attacked by the tubercle bacillus Cases of aseptic necrosis are analogous in so far as the necrosis of the bone marrow is certainly followed by the formation or liberation of toxins in the tissues The surrounding living bone marrow is stimulated by the toxins to mild bone production Thus,

Fig. 2. The tuberculous abscess, C, which contains a cartilaginous, E, and bony sequestrum, F, is surrounded by granulation tissue, D. The abscess lies in the intervertebral space, bounded above and below by adjacent vertebral body borders, B, B2, anteriorly by the anterior longitudinal ligament, A, and posteriorly by fibrous tissue, G, occupying the intervertebral space.

Fig. 3. The osteosclerosis of the bony trabecule occurs by gradual stages as indicated by the cement, A, and apposition, B, lines. Quiescence is indicated by the healing osteoid layer or Gewebeschicht, C. The bone marrow is hypercellular, D, and shows atrophy of the fat cells, E, with fibrosis, F.

quite typically foci of aseptic necrosis are surrounded by a zone of moderate osteosclerosis due to apposition of new bony layers on the surfaces of the old necrotic trabeculæ. However this zone of osteosclerosis is relatively slight and never attains the marked degree observed in this case.

The third possibility is the production of toxins by the tubercle bacillus. This organism does not produce exotoxins, so the sclerosis cannot be the reaction to a vital toxic product of the bacillus. However the tubercle bacillus does contain an endotoxin which is well enshelled in its wax capsule. On necrosis of the organism the toxic irritants are liberated. This concept adequately explains the source of an irritant capable of stimulating bone marrow to marked osteogenesis. This theory is therefore held to be the most feasible one.

SPECIAL STUDIES

The tuberculous abscess. The study of abscess formation in this case is interesting because of the close relationship of these areas of infection to the changes in the other tissues. The abscess cavities which extend along the anterior surface of the vertebral bodies are very narrow and are surrounded on either side by non-specific granulation tissue (Fig. 2, D). The anterior longitudinal ligament delineates the anterior abscess wall while the posterior wall is formed by the eroded bony trabecule, whose bone marrow is condensed where the anterior bony lamellæ of the vertebræ are interrupted. The extension of the prevertebral abscess across the intervertebral space separates the annulus fibrosus of the disc from the anterior longitudinal ligament. The fibers of the ligament are quite frequently split into thinner bundles by invasion of looser connective tissue showing chronic round cell infiltration. The lymphocytes predominate, but a great number of pigment containing histiocytes are also present. They are isolated, frankly wandering or accumulated in small groups. These cells are heavily laden with dark brown pigment evidently hemosiderin, following resorption and organization of hemorrhage. The long duration of the process is indicated by the absence of any free hematogenous pigment in the tissue.

This picture represents an anterior superficial tuberculous spondylitis due to extension of a prevertebral abscess. The pus cavity however shows no signs of activity and is actually shrinking. In some places secondary fibrous tissue obliteration of the abscess occurs by reattachment of the anterior longitudinal ligament to the anterior bone surface. A few foreign body giant cells are seen in the

Fig 4 At the borderline, A, between fatty and hematopoietic bone marrow the fat cells become more prominent. The atrophic fat cells, *B*, show the typical halo of edema. The bony trabeculæ are sclerotic, *D*, in the region of fatty and fibrous bone marrow, but are definitely porotic, *E*, in the areas of myelogenous bone marrow, *C*

Fig 5 The borderline, *A*, between fatty and hematopoietic bone marrow is well defined The fat cells, *B*, become prominent as the myelogenous elements, *D*, begin to fade The halo of edema is seen surrounding the atrophic fat cells, *C*

granulation tissue, but no tubercles are demonstrable

Anterior to several of the intervertebral spaces small fragments of the hyaline cartilaginous terminal layer of the intervertebral discs are found included in necrotic purulent exudate (Fig 2, *E*) In some areas the fragments show marked lacunar outline, some are still undergoing resorption by the fibrous tissue, which also invades the abscess cavity in an attempt to organize the exudate The hyaline cartilage, which is alive, becomes resorbed by a slow cellular process The cartilaginous cell cavities are disrupted, but the intercellular septa of ground substance remain intact for some time

The abscess reveals its most marked effects in the region of destruction of the first lumbar vertebra, where a small bony sequestrum lies in a large, irregular abscess cavity occupying the intervertebral space The adjacent layer of tuberculous granulation tissue, which covers the surface of the eroded sequestrum, has free connection with the caseous material in its marrow spaces In one place the tuberculous granulation tissue is seen invading caseous material in an attempt to resorb and organize it which suggests that tuberculous sequestra can gradually be resorbed by granulation tissue without undergoing molecular disintegration

The tuberculous granulations show marked differences on the two surfaces of the wedge-shaped vertebra from which the sequestrum derived The lower surface presents a picture of quiescence The overlying fibrous tissue is compact, the bony trabeculæ, the surfaces of which are relatively smooth, show condensation and sclerosis On the upper surface, however, the tuberculous process is progressive The fibrous bone marrow is exposed to the intervertebral abscess cavity and has no protective fibrous tissue wall As the fibrous bone marrow becomes denuded, it undergoes necrosis and later infection by tubercle bacilli This area shows a large number of tubercles with giant cells, caseation develops along the irregular surface The trabeculæ undergo extensive osteoclastic bone resorption, there are practically no signs of bone apposition present

The posterior vertebral abscesses present many features similar to those in front, in places they elevate the posterior longitudinal ligament and force it toward the spinal canal The posterior abscess formation, as a whole, is smaller than the anterior, but it extends farther down and at its lower end is relatively large At the inferior aspect, the reactive changes in the marrow extend very far an-

Fig 6 Three young miliary epithelioid tubercles, A are seen lying in hematopoietic bone marrow C T other tubercles, B showing tendency to confluence contain giant cells, On the right a portion of the terminal hyaline cartilaginous layer of the intervertebral disc, D is seen.

Fig 7 This scaldiagram illustrates the relative frequency of miliary tubercles, A as represented by small circles, in the uncolored myelogenous bone marrow B Only single tubercle C is seen in the shaded marrow spaces representing fibrous bone marrow D The contrast between porotic, E and sclerotic, F bony trabecule also brought out The photomicrograph of this section is seen (reversed) in Figure 8

teriorly from the posterior abscess site This signifies that at this level an accumulation of highly toxic tuberculous pus must have been present In one place the posterior longitudinal ligament is still firmly connected to the vertebral surface but the posterior cortex is broken down by extensive osteoclastic bone resorption Furthermore the bone marrow is melting down to give a typical picture of caseation. These very pronounced changes along the posterior surfaces of the vertebral bodies suggest the likelihood of spinal cord involvement but clinically there was no evidence of cord involvement.

Although no signs of any abscesses were present on the anterior side at the same lumbar level, an old abscess cavity included in the anterior part of the intervertebral disc indicates that infection descended to this region (Figs 8 D and 9) This abscess (Fig 9) which is filled with necrotic exudate, is surrounded superficially by a fairly smooth layer of granulation tissue still infiltrated with lymphocytes.

Fibrous tissue Fibrous tissue plays an interesting and important rôle in the process of healing The connective tissue filling the intervertebral space is the product of organization of the preceding abscess by granulation tissue, which is later followed by scar tissue This is illustrated in areas in which the fibrous tissue in the intervertebral space still shows dense lymphocytic infiltration and hyperemia Posteriorly where the space is relatively large the fibrous tissue includes an area which is filled with fibrinous exudate which is undergoing organization by non-specific granulation tissue.

Although some of the intervertebral fibrous tissue is derived from the prevertebral and retrovertebral connective tissue, the greater part arises from the open marrow spaces of the vertebral bodies The marrow spaces which are generally filled with a loose fibrous tissue are open toward the intervertebral space so that the connective tissue fibers of the two areas are in direct continuity with each other The fibers which are protected by trabecule in the deeper bony layers are loosely joined and irregularly arranged no static order prevails However we find that as the fibrous tissue fibers lose their bony protection in the region of mechanical irritation, they become more compact and assume a direction which is parallel to the surface of the intervertebral space

The effect of mechanical irritation on the structure of fibrous tissue can be demonstrated clearly at the intervertebral surfaces of the vertebral bodies The motion which persists between the two eroded bony surfaces subjected the fibrous tissue in the intervertebral space to pressure a gliding component probably added tension stresses As a result of this mechanical irritation of fibrous tissue, a

Fig 8 The contrast between fibrous, *A*, and hematopoietic, *B*, bone marrow is nicely demonstrated The difference between sclerotic, *E*, and porotic, *F*, bony trabeculæ is correspondingly great Degenerative changes are seen in the intervertebral disc, *C* which includes a healed abscess, *D*, anteriorly

definite layer of dense connective tissue is formed at each vertebral surface Between these two compact layers, the fibrous tissue fibers are loosely and irregularly arranged (Fig 10) This picture imitates to a certain degree the structure of an intervertebral disc which normally has a larger central portion of loose, irregular fibrous tissue included between two more compact layers formed by hyaline cartilage Therefore, under very marked pathological conditions the same mechanical factor, especially pressure, which helps in the destruction of the involved intervertebral disc may be the agent which makes an attempt to "re-create" a new disc from simple fibrous tissue

Intervertebral discs The intervertebral discs in areas in which destruction is limited show degenerative changes compatible with the age of the patient Furthermore, this degeneration, which is not specific, is to be expected in view of the altered statics and function of the destroyed vertebral bodies The typical changes in the discs are albumoid degeneration of the fibrous cartilage with characteristic fissuring and cyst formation However, in one place signs of an old abscess are seen in the anterior portion of the intervertebral disc (Fig 8, *D*), while posteriorly there are degenerative changes with small fissures, cysts, and substitution of fibrous cartilage by simple connective tissue The terminal hyaline cartilaginous layers undergo extensive resorption from the underlying bone marrow spaces This is a slow process without much participation of fibrous tissue or multinuclear cells

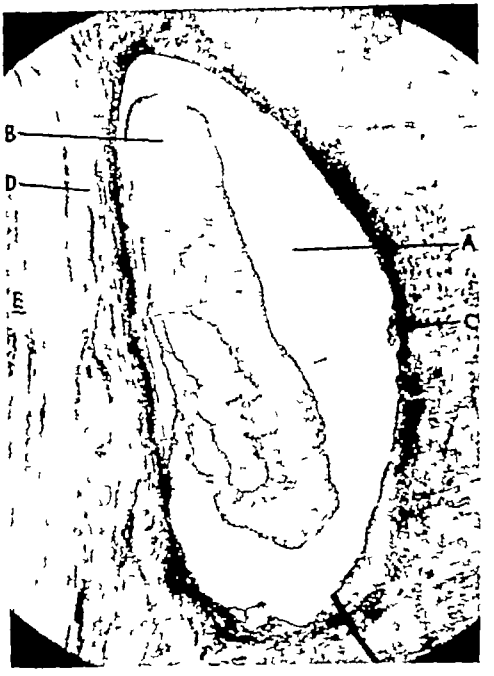

Fig 9 The abscess cavity, *A*, contains a necrotic exudate, *B* The abscess wall is formed by an inner smooth layer of granulation tissue, *C*, and an outer denser layer of scar tissue, *D*, still infiltrated with lymphocytes The anterior fibrous layer of the abscess wall merges with the fibers of the anterior longitudinal ligament, *E*

This picture, which is typical of smooth resorption by mononuclear cells, is seen frequently in cases of atrophy resulting from disuse

The greatest amount of destruction occurs between the twelfth dorsal and first lumbar vertebræ where the intervertebral disc, including its cartilaginous terminal layers, is entirely gone The intervertebral space is transformed into a pus cavity with walls formed by tuberculous granulation tissue undergoing necrosis in its deeper layers However, the vertebral body has not lost much height, the inclusion of a small island of cartilage from the calcified hyaline cartilaginous layer of the disc is seen near the surface of the bone, indicating that the bone tissue has not receded materially in respect to its former relation to the disc Although the intervertebral space immediately superior has been completely obliterated by bony fusion, a similar small inclusion of hyaline non-calcified and calcified cartilaginous tissue is seen in the spongy bone

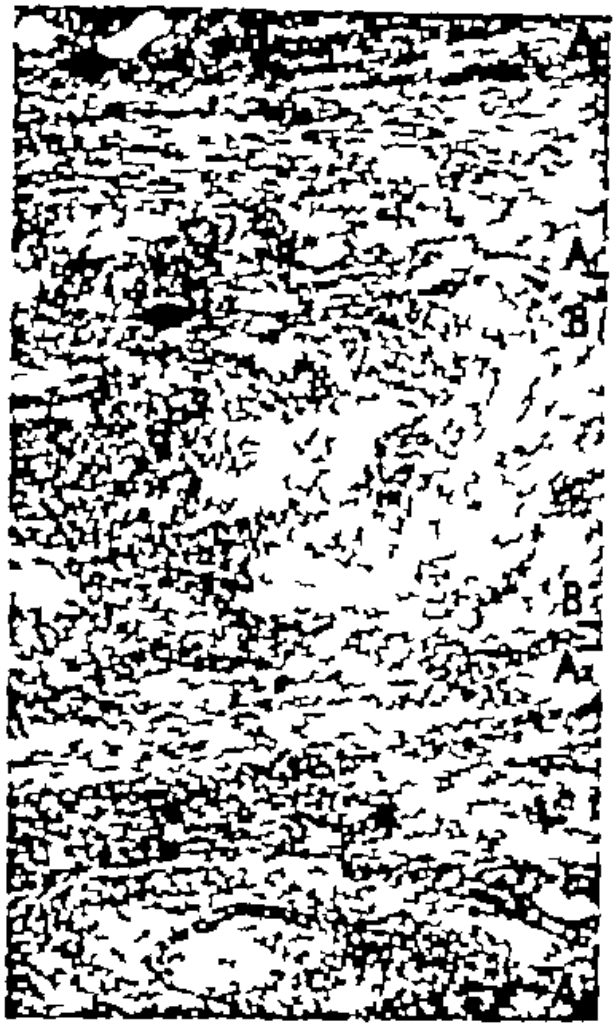

Fig 10 The attempt at transformation of simple fibrous tissue into a primitive intervertebral disc is shown here The upper and lower zones, *A A1* represent dense connective tissue whose fibers run horizontally, parallel to the intervertebral surfaces of the vertebral bodies Centrally the fibrous tissue, *B* is loosely constructed and irregularly arranged

close to the posterior defect in the vertebra. These islands are portions of the hyaline cartilaginous lamellæ which survived destruction of the intervertebral disc. They serve to mark the site of the intervertebral space now obliterated by the bony fusion of the involved vertebræ

The method by which the intervertebral disc heals after infection is shown nicely in several places The abscess which detaches the anterior longitudinal ligament from the intervertebral disc also protrudes into a concave defect in the disc Thus the anterior portion of the disc is formed by dense fibrous tissue which shows a considerable number of blood vessels in its interstitial spaces. This fibrous tissue indicates that the anterior part

Fig 1 This photomacrograph represents the bony fusion between the eleventh and twelfth dorsal vertebræ The line of union is indicated by the transverse direction of the bony trabeculæ, *A* Posteriorly the trabeculæ are assuming the new vertical direction, *B* according to mechanic-static stresses *Fibrosis of bone marrow C* is shown in relation to the line of bony fusion, the posterior defect *D* and the intervertebral abscess, *E*, behind the anterior longitudinal ligament, *F* *Osteosclerosis of bony trabeculæ, G* prevails in these areas, whereas osteoporosis, *I* is marked in the remaining areas of hematopoietic bone marrow *H*

of the disc has been destroyed for a considerable distance from the anterior ligament. However as the abscess began to shrink under organization from the periphery the defect in the intervertebral disc also became smaller by filling up with connective tissue. In the first stages, this fibrous tissue certainly was only granulation tissue later it changed to denser connective tissue, rich in blood vessels This connective tissue therefore represents a scarred defect in the intervertebral disc after the process of healing has progressed for some time.

Bone healing The healing process heretofore was expressed by sclerosis of bony trabeculæ by gradual apposition of layers. Quiescence was recognized by the smooth, blue outline on the surfaces of the bony trabeculæ Other expressions of healing are seen in the bony fusion of vertebral bodies and in the attempt to sequestrate and resorb dead bone tissue.

Bony union following tuberculous destruction is illustrated very nicely by the fusion of the eleventh and twelfth dorsal vertebræ (Fig 11) The union is absolute and the marrow spaces of one vertebral body communicate freely with those of the other Nevertheless, the line of fusion is easily detected by the arrangement of the bony trabeculæ and some peculiarities of the bone marrow The trabec

ulæ, which are quite sclerotic in this region, are arranged in several layers parallel to the horizontal plane of the vertebral bodies This is the method by which the occlusion of the marrow spaces along intervertebral space occurs For some time after bony union these transverse bony lamellæ escape resorption, ultimately, however, they do become resorbed In some places bony resorption is already more advanced, and the bony trabeculæ, which are more uniform in structure, are arranged according to mechanical static demands

The formation of a typical tuberculous sequestrum of spongy bone is seen anterior to the wedge-shaped body of the first lumbar vertebra The bony trabeculæ are entirely necrotic and relatively dense, their surfaces in most places are sharply lacunar The bone marrow consists of a caseous material with partial calcification and caryorrhexis Although the single bony trabeculæ of the sequestrum are of much greater density than those in the porotic areas of the spine, nevertheless, they are not nearly as sclerotic as those trabeculæ in the areas with fibrous bone marrow

Furthermore, the necrotic trabeculæ show less complex structure than the sclerotic trabeculæ This sequestrum, therefore, is evidently a portion remaining from the time when the bone tissue had not yet become so markedly porotic, and at which time osteosclerosis had not yet developed in the bone marrow This sequestrum, no doubt, is very old, dating back to the primary tuberculous necrosis of a portion of the vertebral body when the bony structure was still of normal density Some lacunar resorption had taken place at the surface of the bony trabeculæ as an early response to the infection, but shortly afterwards the bone marrow became caseated, thenceforth, all transforming processes stopped At present, however, the granulation tissue which lies next to the sequestrum is seen invading the caseous marrow spaces in an attempt to resorb and organize it This picture illustrates the fact that tuberculous sequestra may be resorbed gradually by granulation tissue without undergoing molecular deterioration

SUMMARY

Healing, as it occurs in an old case of tuberculous spondylitis, is presented in its various manifestations Bone marrow is stimulated to fibrosis and osteogenesis by irritating toxic substances, which are liberated by necrosis of tubercle bacilli Fibrosis develops after the hematopoietic bone marrow loses its specific elements and after the fatty bone marrow undergoes atrophy of the fat cells The bony trabeculæ are markedly sclerotic in the regions of fibrous bone marrow, less dense in the fatty marrow, and actually porotic in regions of normal hematopoietic bone marrow These findings are explained thus near a focus of destruction there is a greater concentration of toxins and therefore greater irritation of nearby bone marrow which responds by fibrosis and osteogenesis As the distance from the point of toxin production increases, the damaging substances become more dilute and the bone tissues react to a much less marked degree The possibility of mechanical irritation or pyogenic infection as the cause of fibrosis and sclerosis is considered insignificant in this case Bone healing is further manifested by bony fusion of the vertebræ and by the elimination of tuberculous necrotic bone areas

The tissues which react to toxin irritation by fibrosis also acquire an increased resistance to infection by the tubercle bacillus Evidence to substantiate this statement is furnished by the ability of miliary tubercles to invade myelogenous bone marrow and their inability to develop in places where the marrow spaces are filled with fibrous tissue It is assumed that the fibrous marrow, after prolonged exposure to tuberculous toxins acquired a rather high immunity to the disease Therefore, when a miliary dissemination occurred shortly before the patient's death, the immune fibrotic areas withstood the fresh invasion and no young tubercles developed The more remote regions, however, did not receive the benefit of inoculation with toxins, as a result the tubercle bacilli found susceptible tissue in the regions of hematopoietic bone marrow, where young tubercles are seen with relative frequency

Although the general picture is one of ques-

cence of the tuberculous process, certain areas show activity osteoclasia occurs in relation to abscesses and traumatization Fibrous tissue develops in an attempt to organize abscesses and even invades the caseous tissue of a tuberculous sequestrum in an attempt to resorb and organize it. The infection in the intervertebral discs heals by fibrous tissue scarring In some places motion persists in the intervertebral space after destruction of the disc, and by mechanical irritation tends to transform simple fibrous tissue into a primitive intervertebral disc

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ANESTHESIA AND BLOOD LIPIDS[1]

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THE effect of anesthesia upon the concentration of blood lipids has been studied frequently in the lower animals, less frequently in man The changes encountered among the lower animals vary from one species of animal to another, which may be shown to explain many of the apparent discrepancies in the conclusions of earlier investigators This variation between species also exemplifies the older fallacy of assuming that changes which occur in animals likewise occur in man In several contributions to this subject, it has been tacitly taken for granted that the demonstration of an increase in one of the blood lipids may be taken as *a priori* evidence that all of the lipids vary in the same direction Although frequently the case, such a relationship need not always hold In but a few cases has a complete differential lipid analysis of blood been performed before and after anesthesia due largely to the previous lack of sufficiently micro-methods for lipid estimation Practically all of the previous work on anesthesia has been performed with whole blood Since variations in the lipid composition of plasma are seldom the same as those in the red blood cells (7, 9, 11, 12), it follows that analysis of whole blood alone will indicate most inadequately the actual variations in blood. For these reasons it was felt that there was needed a systematic survey of *all* the lipids in *both* plasma and the red blood cells in the human subject when under the influence of anesthesia

The earliest and one of the most thorough investigations in this field was that of Karl Reicher in 1908 Reicher demonstrated that ether, chloroform, and various other narcotics produced in dogs an increase in the *Alkohol-Aetherextrakt, Fett, Lezithin, Cholesterin*, and *Frei Fettsaeuren* of whole blood These observations were subsequently confirmed in whole or in part by Bloor, Mann, Bang, Berczeller, Ducceshi, Biasini, Hospers, and Prochnow and Findeisen Murlin and Riche stated that ether, chloretone, and morphine lowered blood fat as estimated nephelometrically, while Lattes recorded inconstant changes after chloroform anesthesia At this point it may be noted that certain narcotic drugs have different effects which may be due in part to a time factor or to specific difference in the effect of the drug The results recorded above have been those obtained with ether Chloroform also causes a lipemia in dogs but it may not appear for several days, the "after rise" of Bloor Morphine and alcohol (1, 4) and ethylene and nitrous oxide (20) apparently have little effect

In contrast to the lipemia caused by ether anesthesia in dogs, Robinson has found that ether produces a consistent *decrease* in the cholesterol content of cat's blood

Experiments with rabbits have uniformly shown that ether and chloroform anesthesia induce a lipemia due to an increase in cholesterol (17, 19, 20, 22), phospholipids (22) and total fatty acids (1, 22) According to Gray, paraldehyde and urethane have no consistent effect in the rabbit, but Ghose found that a fatal dose of urethane would also cause a lipemia Bang reported that alcohol produced a marked lipemia

Manceau has recorded a few observations on the changes in the guinea pig following chloroform narcosis, in which, curiously, he found blood cholesterol was increased but lecithin unchanged or decreased

The conclusions of those who have investigated anesthesia in the human subject are in striking discord the one with the other Blood cholesterol has been variously reported to be lowered (18), little changed (14), or increased (16, 25) When the total lipid alone was analysed, it was generally found to exhibit insignificant increases or no change (21, 35), but Prochnow and Findeisen (30) found that ether narcosis doubled the *Blutfette* Von Seemen (33) recorded an initial lipemia followed by a lipopenia (for use of the term,

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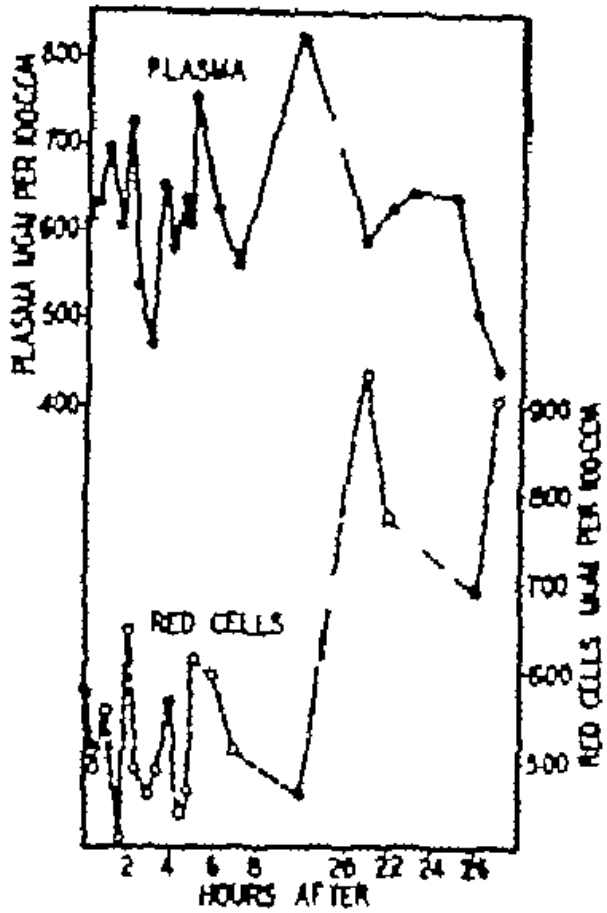

Fig. The effect of anesthesia on the concentration of total lipid in plasma and the red blood cells

lipopenia see Boyd 9) and later a return to normal in 13 cases In serum the *Bloffette* has been found to be increased by Popper and Scholl (29) Blood phospholipids have received little attention but MacKay (24) demonstrated a distinct increase in inorganic phosphorus Evipan and spinal anesthesia (16) and local anesthesia (30) have not been found to affect blood lipids in man

METHOD

All cases studied were from the gynecological divisions of the Strong Memorial Hospital They were selected with a view to studying only those in which an anesthetic was to be given for some time and in which the operation to be performed involved a minimum of tissue injury and hemorrhage As most of the cases were used for class demonstrations and pelvic examinations, an anesthetic was given for at least 1 hour Except for a few instances of major operations, the surgical interference was of a minor character such as a dilatation and curettage of the uterus Twenty cases were studied They received the usual pre-operative narcotic, atropine and morphine Anesthesia was induced with nitrous oxide and oxygen and continued with ether

Blood was taken from the arm veins before operation and again at an interval of from 1 to 27 hours after operation. The blood was oxalated and immediately centrifuged. Plasma was extracted and analyzed by Bloor oxidative micro-methods as modified by Boyd (5, 6 8 10) The red cells were first laked with a minimal amount of distilled water then extracted with alcohol-ether and analyzed in the same manner as plasma

RESULTS

Two samples of blood were secured from each of the 20 subjects and from each sample of blood two extracts were prepared, one of plasma and one of the red blood cells. In each extract the following lipid values were estimated total lipid, neutral fat, total fatty acids phospholipid fatty acids, neutral fat fatty acids, cholesterol ester fatty acids, total cholesterol, ester cholesterol free cholesterol, and phospholipid In most of the extracts, iodine numbers were also determined for the phospholipid fatty acids and the non-phospholipid fatty acids both in plasma and in the red cells In all, upward of one thousand lipid values were obtained

To prepare this information in a readily digestible form offered some difficulty Only the essential or "key" values have been presented. From the data given in Figures 1 to 5, values for the remaining lipids as already listed may be calculated using the factors evaluated by Boyd (6) Figures 1 to 7 are offered as general anesthesia curves The starting point of each curve represents the mean value of that particular lipid before an anesthetic was given Subsequent points represent values obtained in individual cases at the postoperative hours indicated. To avoid overlapping of curves, separate ordinates for plasma and the red cells have been used in most instances

Total lipid (Fig 1) In plasma, no consistent change took place in the value of total

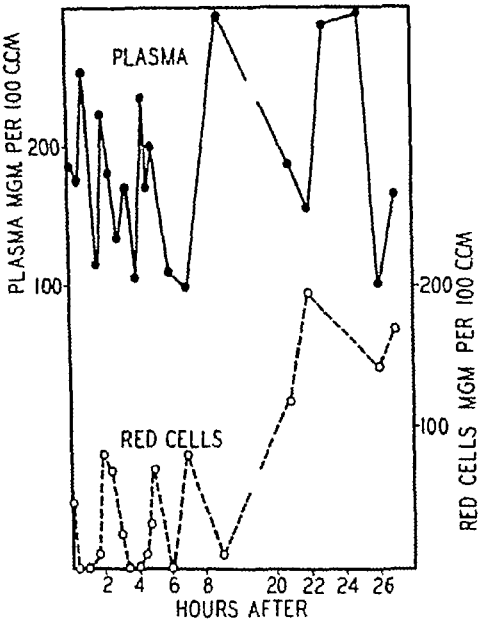

Fig 2 The effect of anesthesia on the concentration of neutral fat in plasma and the red blood cells

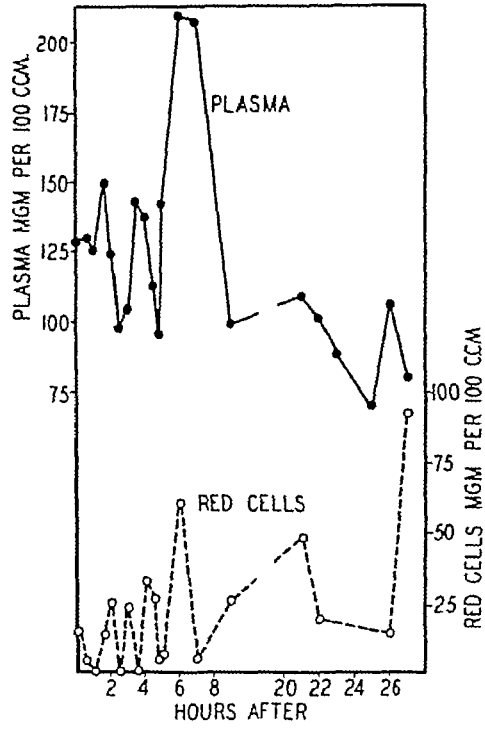

Fig 3 The effect of anesthesia on the concentration of ester cholesterol in plasma and the red blood cells

lipid until 24 hours had passed when there was a tendency toward decreasing values Such occurred in 4 of 6 cases examined at about the 24 hour period In 11 of 14 cases, total lipid was lowered in the red cells during the hours immediately following anesthesia The next morning, however, all cases exhibited a striking increase in the lipid content of the erythrocytes

As a net result, the lipid content of whole blood (calculated from the hematocrit readings in conjunction with the above data) decreased immediately following anesthesia, constituting a lipopenia, and increased in 24 hours or so, constituting a lipemia The interesting feature of this lipemia of anesthesia is that it was unlike any other lipemia which, to the best of the author's knowledge, has been heretofore described In all the known lipemias, lipids are increased both in plasma and the red cells or, more commonly, in plasma alone The anesthetic lipemia was due to an increase in the lipid content of the red cells, an increase sufficient to offset a slight actual decrease in the plasma lipids

Neutral fat (*Fig 2*) Neutral fat exhibited a comparatively minor rôle in plasma In 14 of the 20 cases, plasma neutral fat declined in value without any apparent relation to time In the red cells, there was an early decline in the concentration of neutral fat in 10 of 14 cases and this, together with the decrease in plasma, accounted for a major portion of the early lipopenia of anesthesia The superseding lipemia may also be seen to be due in part to a marked rise in the neutral fat of the red blood cells

The author and H J Tweddell have recently found that there is a diurnal variation in the neutral fat content of the red cells (13) In this work, cellular neutral fat was found to be increased between 8 a m and 5 p m Under anesthesia, however, cellular neutral fat declined during this period since most of the operations began at 8 a m to 9 a m It cannot be gainsaid that the increase the morning after anesthesia may not have been partly due to diurnal variation The extent of diurnal change was much less than that produced by the anesthetic. Altogether, the

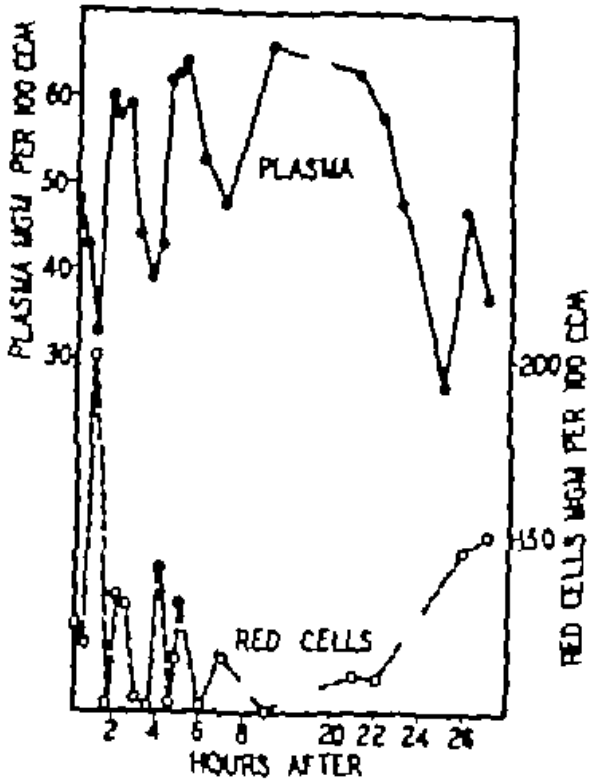

Fig 4 The effect of anesthesia on the concentration of free cholesterol in plasma and the red blood cells

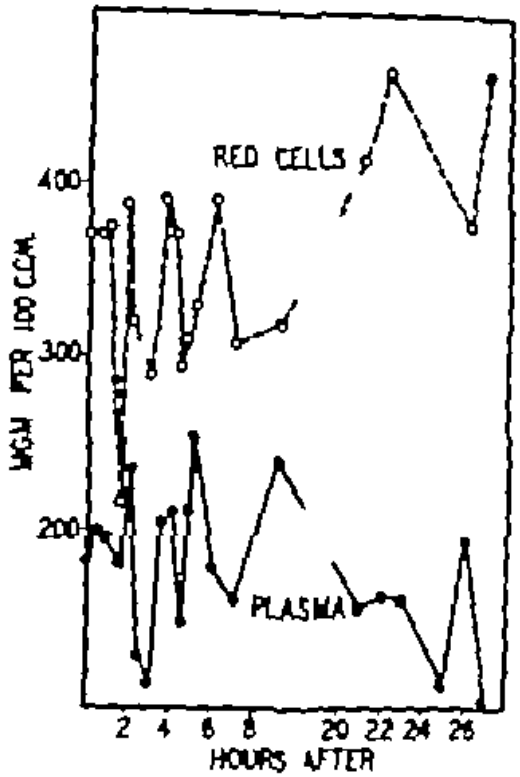

Fig 5 The effect of anesthesia on the concentration of phospholipid in plasma and the red blood cells

changes herein recorded for neutral fat appear to be due largely if not entirely to the effect of the anesthesia

Ester cholesterol (*Fig 3*) The significant change in plasma ester cholesterol occurred 24 hours after anesthesia. Immediately after the narcosis, the plasma ester cholesterol *fluctuated in value but showed no uniform* trends. By the next morning all values in all cases were lower than the initial values, many markedly so In the red blood cells, half of the cases exhibited an immediate augmentation and half an immediate diminution in the percentage of ester cholesterol There were indications that the erythrocytes at 24 hours tended to have somewhat larger amounts of ester cholesterol, but in view of the low values and the marked variation little significance can be attached to changes in the ester cholesterol of the red cells

Free cholesterol (*Fig 4*) Although plasma ester cholesterol showed no definite changes immediately after anesthesia, free cholesterol was definitely increased in 9 of 14 cases studied at this time the change being well represented in Figure 4 From the point of view of lipid metabolism, this again is a remarkable occurrence. Of all the blood lipids, the author has invariably found free cholesterol to exhibit the least tendency to vary in health or disease (7 9, 10 11) Yet here is a situation in which free cholesterol changes and ester cholesterol does not It is possible that the results may be interpreted as signifying that anesthesia has an effect on sterol metabolism apart from the rôle played by sterols and sterol esters in lipid metabolism There were no obvious changes in the free cholesterol of the red blood cells

Phospholipids (*Fig 5*) The phospholipid content of plasma gave no evidence of significant changes within 9 hours of the period of anesthetic administration By 21 to 27 hours, it tended to be lower in most cases. The phospholipid of the red cells fell in value in 10 of 14 cases immediately after anesthesia but rose to high concentrations at the later period in all cases then studied. These results were analogous to those noted for neutral fat and ester cholesterol and together with them explain the changes encountered in the total lipid curves of Figure 1

Iodine number of the phospholipid fatty acids (*Fig 6*) Iodine numbers of the phospholipid

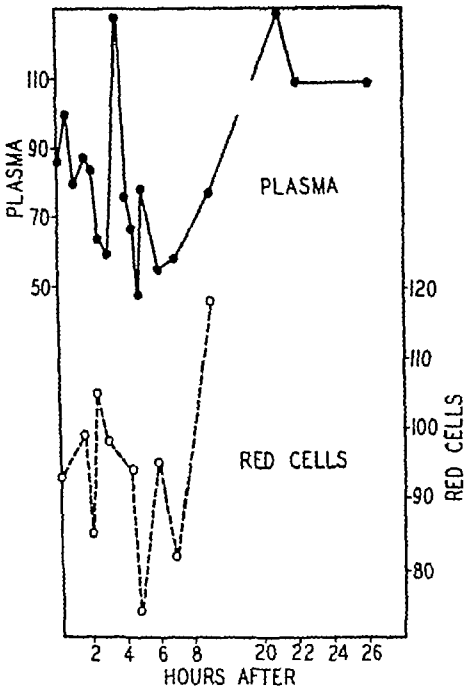

Fig 6 The effect of anesthesia on the iodine number of the phospholipid fatty acids in plasma and the red blood cells

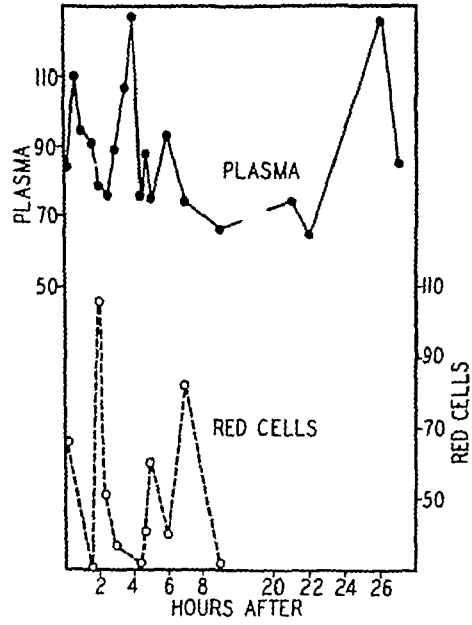

Fig 7 The effect of anesthesia on the iodine number of the non-phospholipid fatty acids in plasma and the red blood cells

fatty acids were determined in order to ascertain if variations in the composition of the phospholipids accompanied variations in their concentration The phospholipids, isolated by acetone-magnesium chloride precipitation, were dissolved in hot alcohol and saponified The fatty acids were then taken up first in hot petroleum ether and then in chloroform and their iodine number determined

As shown in Figure 6, immediately after anesthesia the iodine number of the phospholipid fatty acids in plasma tended to decline (11 of 14 cases) while that of the red cells increased (6 of 9 cases) The results suggest that phospholipids containing the more saturated fatty acids tend to diffuse out of the red cells immediately after anesthesia, since the total phospholipid of the red cells has been shown to decrease in amount at this time These cellular phospholipids apparently do not remain in plasma but are removed along with similar saturated phospholipids from plasma in the later 21 to 27 hour period, leaving in plasma a lowered percentage of phospholipid and that of a higher iodine number This absorption by body tissues from plasma of relatively saturated phospholipids is of interest in view of Sinclair's postulate that such types of phospholipid (i e with low iodine numbers) are probably the types used in metabolism as against the high iodine number phospholipids which, according to Sinclair, are probably related chiefly to the structural make-up of cells

Iodine number of the non-phospholipid fatty acids (Fig 7) That portion of the total lipid remaining in the acetone-petroleum ether mother liquor after precipitation of the phospholipids was re-dissolved in hot alcohol, saponified, and the iodine number of the resulting non-phospholipid fatty acids determined after subtracting the iodine absorption value of the cholesterol present

The non-phospholipid fatty acids are comprised of fatty acids derived from neutral fat and cholesterol esters Immediately after anesthesia there has been shown to be no significant change in the amount of these lipids in plasma and, as seen in Figure 7, there was likewise no significant change in

composition as evidenced by iodine numbers In the red cells at this time, 8 of the 10 cases exhibited a lowered iodine number which again suggests that the lipids of the red cells are taking some active part in fat metabolism at this time

RECAPITULATION

By grouping the effect of anesthesia according to species of animal, it has been found that the results of the major portion of previous investigations may be shown to be in harmony the one with the other in spite of an apparent superficial discord. In the dog and rabbit, inhalation anesthesia produces a lipemia. The cat and the guinea pig have been insufficiently studied to warrant a final statement. Research on blood lipids during anesthesia in man has given rise to conflicting deductions but the present investigation has explained some, possibly all, of the discrepancies It has been shown that the effect of inhalation anesthesia in the human varies at different periods after operation And it has been shown that changes in the red blood cells differ both in nature and amount from those in plasma.

Briefly within the first 8 to 10 hours of the postanesthetic period in the human, there occurs a lipopenia or decreased concentration of blood lipids (for use of the term, lipopenia, see Boyd, 9) This initial lipopenia was shown to be due to (a) a decrease in neutral fat of both plasma and the red cells and (b) a decrease in the phospholipid of the red cells Some 21 to 27 hours after the anesthesia, the lipopenic period gives way to a second period characterized by a lipemia This lipemia was shown to be due to (a) a marked increase in the neutral fat of the red cells, (b) a definite though less marked increase in the phospholipid of the red cells, and (c) a slight and more variable rise in the ester cholesterol content of the erythrocytes.

It will be noted that both the lipopenia and the lipemia owe their origin largely to changes which took place in the red cells In fact, the lipopenic period was characterized by increasing percentages of plasma free cholesterol and the lipemic period by decreasing amounts of plasma free cholesterol, ester cholesterol, and phospholipid. The quantitative changes in the plasma lipids were opposite to those in the red cells in both periods although not involving corresponding lipids in each with the partial exception of phospholipid The fact that the quantitative change in the red cells was greater than that in plasma enabled the red cells to be the determining factor in differentiating the periods as first lipopenic and second lipemic. As noted before, the author believes this to be the first recorded instance of a lipemia being due to increased amounts of lipids in the red cells alone.

A criticism which might possibly be applied to the results as recorded to this point is that the changes in the lipid content of the red cells might be due to changes in their volume, especially since the amount of cellular lipid has been expressed as units per volume. In reply to this, it may be noted that in practically all of the cases studied blood loss was at a minimum during operation and hence the changes recorded were undoubtedly due, for the most part if not entirely to the effect of the anesthetic. Webster has shown that anesthesia does not produce any change in the volume of the red blood cells. While Webster's results appeared sufficiently conclusive his general technique was applied to all of the cases herein studied and results obtained which confirmed his statements and at the same time proved that the results of the present investigation were real and not apparent

SUMMARY

In 20 cases of minor gynecological operations the effect of nitrous oxide-ether anesthesia on the concentration of lipids in plasma and the red blood cells was determined by oxidative micro-methods

Within the first 8 to 10 hours, a lipopenia developed due to a decrease in the neutral fat and phospholipid of the red blood cells and a fall in plasma neutral fat. This was followed by a lipemia about 24 hours after the anesthetic and the lipemia was due to a marked increase in the neutral fat, phospholipid and cholesterol esters of the red blood cells, the cholesterol fractions and phospholipid of plasma being slightly decreased in value. The unusual nature of this lipemia has been noted.

From iodine number studies, plasma was found to contain more saturated phospholipids during the lipopenia and more unsaturated phospholipids during the lipemia, the red cells discharging their saturated phospholipids in the lipopenic period The neutral fat and cholesterol esters of the red cells became more unsaturated under the influence of anesthesia while in plasma no change occurred

Plasma free cholesterol increased in value during the lipopenic stage while ester cholesterol did not, suggesting that anesthesia affects sterol metabolism independently of its effect through the intermediary of lipid metabolism

The results were shown to explain many of the discrepancies in earlier studies on man, while grouping earlier data according to species served to bring into harmony certain discordant conclusions among animal studies

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CHOLANGIOGRAPHY

A Modified Technique for the X ray Visualization of the Bile Ducts During Operation[1]

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THE purpose of this paper is to present a method for the visualization of the biliary ducts while the patient is on the operating table and without opening the common duct.

The difficulties inherent in surgery of the biliary tract are increased by the wide variation in the clinical manifestations of common duct obstruction the anatomical arrangement of the biliary ducts, and pathological changes which are difficult of interpretation. Consequently the indications for choledochotomy are not usually clear except in cases presenting a typical history of common duct obstruction and those in which at the time of operation the bile passages are definitely found to be abnormal

In most patients with symptoms of biliary obstruction, the indications for surgical exploration of the common duct rest upon a consideration of many factors. These indications have been stated by Kehr Eisendrath Labey and others, and have been generally accepted. They are

1 A history of jaundice accompanied by chills or fever

2 Thickened and contracted gall bladder

3 Thickening of the head of the pancreas.

4. Thickening and dilatation of the common duct.

5 Enlargement induration, or cirrhosis of the liver

6 The presence of many small stones in the gall bladder and cystic duct

7 A cystic duct dilated by stones and separated from the common duct with difficulty with a likelihood of spillage of the stones into the common duct.

8. The presence of muddy bile on section of the cystic duct suggestive of inflammation of the common duct.

9 The recurrence of pain or symptoms of cholangitis after operation on the biliary tract.

From the foregoing it is clear that exploration of the bile duct is performed largely on indirect evidence the correct interpretation of which depends upon the experience and diagnostic skill of the individual surgeon. It is easy to understand therefore, why the common duct is opened needlessly in some cases, whereas in others it is not opened when it should be. Unnecessary exploration of the common duct adds to the morbidity and increases the complications of operation, while failure to explore when disease is present renders a second operation necessary for complete relief

Even when the common duct is opened and explored, the surgeon up to the present time has no method of making certain whether or not he has completely removed the obstruction. This not infrequently results in overlooking stones present Under these circumstances secondary operations on the common duct, which are difficult and dangerous, become necessary

In other cases the cause of the obstruction is not recognized, the presence of stone being assumed when stricture or tumor is present. Failure to secure the supposed stone is explained in saying that it has been pushed through the ampulla into the duodenum The gall bladder is then removed, and when the true condition of the patient finally becomes apparent, the opportunity for sidetracking the bile may have been lost. While choledochoduodenostomy is often feasible and transplantations of external biliary fistulas into the stomach or duodenum have been done successfully these operations are attended with a high percentage of failures.

[1] From the Departments of Surgery and Roentgenology of the Beth Israel Hospital Boston, Massachusetts

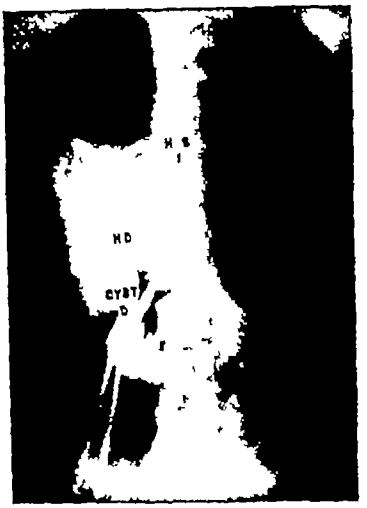

Fig 5 Obstruction (partial) of common duct by stricture *HD*, Hepatic duct. *Cyst D*, Clamp on cystic duct Note dilated hepatic duct and intrahepatic biliary radicles Duodenum well filled with dye revealing patent sphincter Common duct distal to stricture is normal

Fig 6 Visualization of pancreatic duct obtained by injecting common duct during operation Arrow points to pancreatic duct. Pancreas enlarged and indurated

Normal films for comparison were prepared by injecting fresh cadavers, dead as a result of lesions involving organs other than the liver or bile passages, and exposing films according to the same technique as used in the operating room

RESULTS

We have used this method in 25 cases to date In only 1 case did the first film fail to agree with the exploratory findings and check up film In this instance the dye stopped abruptly at the ampulla and failed to enter the duodenum Our impression was that obstruction probably existed at the ampulla, but exploration and check up films revealed the duct and ampulla patent

In 4 instances the pancreatic ducts were visualized It is of interest to note that in each of these 4 cases chronic pancreatitis, as evidenced by enlargement and hardening of the gland, was found on exploration On follow-up these patients continue to complain of symptoms in whole or in part, and we believe, therefore, that this observation is of prognostic significance

No untoward reactions have been encountered to date as a result of injecting hippuran into the bile ducts On several occasions in obtaining check up films after operation by injecting through the drainage tube in the common duct, patients complained of transient epigastric pain radiating to the back, in 1 patient so injected on the ninth postoperative day, fever of a marked degree developed and persisted for 4 or 5 days The fever in this instance was unexplained and may have been coincidental

VALUE OF METHOD

This procedure is intended to furnish information not available by any other diagnostic method in present use Since extremely small stones and so called sand bile will not show on the film, judgment as to what should be done in cases in which the evidence is not clear cut will depend as heretofore on the clinical evaluation of the case arrived at after thorough diagnostic study For this reason, as well as for the technical difficulty associated with roentgenography and the experience necessary in the interpretation of the films, a complete study should not be omitted even if this method is to be employed

The only contra-indication to this procedure which appears to merit consideration is

Fig 1.

Fig 3

Fig 4

Fig 1 Visualization of normal biliary ducts obtained by injection of fresh cadavers Common duct is of average size, regular in shape, and permits free flow of dye into the duodenum

Fig 3 Visualization of normal duct during operation Note size and appearance of common duct as well as free flow of hippuran into duodenum (common duct not opened)

Fig 4 Obstruction of common duct by stone *GB* Clamp on gall bladder *CD* Clamp on cystic duct Arrow points to stones Common duct and hepatic radicles are dilated Small amounts of dye entered duodenum (Stones recovered when duct was opened)

blocking the field and the skin towels for protecting the wound are stitched in place or held with aluminum clips in order to prevent metal shadows from appearing on the film The operation is conducted as usual except that the common duct is identified before the gall bladder is disturbed The cystic duct is then carefully dissected and clamped By means of an ordinary 30 cubic centimeter glass syringe and a 15 to 18 gauge angulated tonsil needle 20 to 25 cubic centimeters of hippuran is then injected into the common duct. A towel is placed over the wound the operator and assistants step aside a portable X ray unit is brought into position and an exposure is made The film is then removed and another one replaced in the drawer The exposed film is quickly developed and the surgeon is able to view it within 6 minutes.

The operation is performed according to the indications revealed by X-ray If the film demonstrates that the common duct is clear and unobstructed, incision and exploration of the duct can be dispensed with. If the film shows obstruction suggesting stone, stricture, or neoplasm, the duct is opened and explored, and the lesion is dealt with accordingly After this procedure is completed a catheter or T tube is inserted in the duct and through it 30 cubic centimeters of hippuran is injected and a second exposure is made. The surgeon is thus able to determine whether or not the obstruction is completely removed. As many exposures as seem necessary may be made If the obstruction cannot be removed as in the case of inoperable stricture or tumor of the duct or the pancreas, the only alternative is to anastomose the gall bladder or common duct if possible, to the stomach or duodenum. When the surgeon is satisfied that his operation is adequate, he can close the peritoneum fully assured there will be no necessity for reoperation for an overlooked stone or stricture

Hippuran[1] is a sterile, aqueous, 40 per cent organic iodine solution it is a harmless substance which is excreted through the kidneys, and has proved satisfactory in every way Various other media were tried but were given up either because of undue viscosity high cost or failure to produce a clear cut roentgenogram.

[1] Mallinckrodt Chemical Co product.

EFFECTS OF VAGOTOMY ON THE GASTRIC FUNCTIONS OF MONKEYS

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SURGICAL interruption of the nerve supply to the stomach has been frequently advocated for diverse disorders including tabetic crises certain "functional disturbances e g pylorospasm, and more recently for peptic ulcers Reference may be made to Exner and Schwarzmann (1914) Latarjet (1922) Pauchet (1923) Gianolla (1923) Hughson (1925), Schiassi (1925) Foa (1927) Klein (1929) Winkelstein (1929) and Berg (1930) Partial gastrectomy has also been advocated as an additional measure to diminish acidity by eliminating part of the secretory epithelium (Portis and Portis 1926), and to produce the inhibitory effects on motility which generally follow a drastic operation of this character (Hughson, 1925) Many failures are on record, such as those of Pieri and his assistants (1930) who presented a well studied series of ulcer cases in which the effects of vagotomy on gastric acidity proved to be but temporary

Data from experimental work on animals indicate that little short of a radical resection of the whole vagal supply, preferably coupled with subtotal gastrectomy, can be relied upon to give a definite lessening of gastric secretion and acidity Even with the combined procedure a positive result is likely to be temporary owing to potent local and humoral compensatory mechanisms

As no detailed physiological analyses of the effects of vagotomy in subhuman primates are to be found in the experimental literature it appeared desirable to undertake such a study in view of the likelihood that experimentation of these higher forms would throw more light on the relevant clinical problems than the classical experiments on dogs and cats McCrea (1926) defended denervation of the stomach for certain gastric affections and our purpose has been to analyze the rationale of such procedures along physiological lines The present study has in fact revealed certain data having a definite bearing on gastric surgery and we propose therefore to describe the experiments briefly and discuss them in detail

METHOD OF STUDY

1 *Operative procedures* During the course of previously reported experiments (27–30) on the gastric anacidity producible in the green monkey (*Cercopithecus aethiops sabaeus*, Schwarz or *Lasiopyga callithrix* Elliot) by parasympathomimetic drugs administered via the brain ventricles and in other ways 10 animals were subjected to bilateral severance of the vagus nerves the operation being performed surgically and the animals allowed to recover In 5 cases the section was made in the neck and in the 5 remaining it was made below the diaphragm via a midline abdominal incision Table I summarizes the operative procedures the complications and the effects of the vagotomy upon (a) the motility of the cardia and (b) the secretion of acid in response to a farina gruel test meal

2 *Anatomical note* In the 10 young green monkeys of this experimental series the right vagus divided in the lower thorax into two branches The anterior branch formed the *anterior abdominal vagus trunk* The posterior branch joined the left vagus to form the *posterior abdominal vagus trunk* In one animal, not included in the present series the left vagus bifurcated and one-half formed the anterior vagal trunk while the whole of the right vagus joined the other branch to form the posterior vagal trunk The subdiaphragmatic approach permitted ready identification of the abdominal nerve trunks for some distance above the point at which the alimentary twigs began to be given off In the neck, the recurrent laryngeal division usually formed a separable nerve bundle—especially on the left side—and every effort was made to spare this in the neck operations, with incomplete success, however

the presence of acute infection in the biliary tract. Theoretically the further dissemination of such infection appears to be a distinct possibility and it is for this reason that we have not employed this method in any such case

Roentgen visualization of the bile ducts according to the technique described interferes in no way with the conduct of the operation. On the contrary by providing the surgeon with visual evidence for determining whether or not the common duct should be opened and if opened whether or not a demonstrated obstruction has been removed It should in our opinion be of considerable value. This is especially true in the case of common duct obstruction due to stone With further experience, it should likewise provide valuable information in such conditions as neoplasm of the bile ducts, neoplasm of the head of the pancreas, hepatic stone cholangitis, diverticula of the bile ducts internal biliary fistula, and stricture

SUMMARY AND CONCLUSIONS

1 A method for the roentgen visualization of the biliary tract during the course of operation is presented

2 This procedure is simple does not interfere with the conduct of the operation is not attended by any untoward reactions and provides valuable information obtainable through no other diagnostic method in present use

3 Twenty five patients have been subjected to this examination. The films in every instance except one accurately visualized the condition present as determined by operation and postoperative study In one instance the data was equivocal.

4. In 4 cases the pancreatic duct was visualized. This occurrence, we believe, is of prognostic significance and will be dealt with in a later communication

5 The only contra-indication to this method appears to be acute infection of the biliary tract.

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Fig 2 Green monkey No 13 (normal), intraventricular injection of pilocarpine (1 0 milligrams per kilogram) a, left, Two minutes after injecting barium meal Note cardiospasm (with retention of meal in esophagus), and "mass emptying" of stomach b, Eight minutes after giving barium meal Note method of gastric emptying, viz , (1) fundus contracts pushing whole of meal into pyloric portion where it is retained by incisural ring, then (2) pylorus opens and antrum is emptied by a series of strong "concentric contractions" (=*mass emptying*)

more marked signs of esophageal obstruction than the subdiaphragmatic section, which suggested (a) that the disintegration of the movements of the thoracic esophagus aggravated the dysphagia, and (b) that the mere fact of operative interference around the cardia and the subsequent adhesions were insufficient to account for the obstruction As might be expected, the local mechanism was still able to handle a more fluid intake and the dysphagia definitely improved, so that the animals which lived long enough eventually gained in weight In view of the earlier data, it seems to us significant, however, that definite evidence of cardiospasm persisted throughout the period of observation, which in some cases was extended over many months The passage of the stomach tube, for the purpose of conducting test meal studies, proved to be a valuable indication of cardiospasm as the obstruction could readily be identified by means of the catheter Further evidence was secured in a few instances by an X-ray examination following a barium meal introduced into the upper esophagus via the catheter The typical constriction at the cardia, with dilation and vigorous peristaltic movements of the gullet, which sometimes returned the food to the mouth, were noted with the fluoroscope The roentgenograms of animal 8, (Fig 1, a, b) show satisfactorily the cardiospasm and long delay in esophageal emptying (Fig 1, b) being taken 40 minutes after the introduction of the meal into the esophagus Autopsy, especially of the animals which died soon after the vagotomy, revealed stricture at the cardio-esophageal junction and the gullet distended with undigested food Figure 3 represents a drawing of this typical condition as encountered in animal 12

Fig 1 Green monkey No 8, 5 days after subdiaphragmatic vagotomy a, left, Barium meal in esophagus (and stomach) 2 minutes after injection via rubber catheter seen in roentgenogram Note cardiospasm and esophageal dilatation, with peristaltic waves b, Residue of barium meal still in esophagus 40 minutes after injection Note gastric atony and absence of stomach emptying.

A full account of the innervation of the stomach is given by McCrea (1926) and Kuntz (1930) Latarjet (1922) gives a valuable contribution from the viewpoint of the surgery of the human gastric nerves.

3 *Postoperative complications* In accordance with the experience of earlier observers on other animals bilateral cervical vagotomy was fraught with grave danger from pulmonary complications (Weiser 1932 1933) The subdiaphragmatic approach proved uniformly satisfactory as far as the general health of the animal was concerned

Of unusual interest was the death of animal 8 on the twentieth day from a *duodenal erosion* which perforated into the pancreas, liberating bile and blood into the upper peritoneal cavity and digesting away the posterior duodenal wall in the affected area. A small erosion on the lesser stomach curvature of animal 5 was discovered incidentally during autopsy It was not accompanied by hemorrhage, although it extended into the muscular coat. The possibility of a postmortem or agonal change was not ruled out in this case. The mucosa of the stomach and rest of the alimentary tract were normal in all the other animals Owing to postmortem changes, neither of the erosions described proved suitable material for histological examination.

OBSERVATIONS AND RESULTS

A *Motility disturbances* 1 *Cardiospasm* In all 10 animals striking evidence of cardiospasm developed after complete vagotomy Unilateral vagotomy in the neck caused no demonstrable effects The lines of evidence were (1) clinical (2) esophageal catheterization, (3) roentgenological and (4) autopsy

The clinical evidence consisted in the typical signs of esophageal obstruction with dysphagia, gurglings, and regurgitation of well chewed but undigested food boli These signs were most marked in the few days after the operation but they could be demonstrated (by feeding with a banana or carrot) for many weeks, in the case of the animals which survived The operation in the neck caused even

TABLE I—SUMMARY OF PROCEDURES CARRIED OUT ON TEN MONKEYS

Animal No	Operation	Postoperative course	Day of death after complete vagotomy	Cause of death	Cardiospasm	Acid tide following test meal
2	One stage (neck)	Downhill	4	Pneumonia	+	No test
5	One stage (neck)	Downhill	3	Pneumonia (gastric erosion)	+	No test
3	Two stage (neck)	Recovered	57	*Intracranial hemorrhage following intraventricular injection	+	+
11	Two stage (neck)	Slowly downhill	10	Pneumonia	+	No test
12	Two stage (neck)	Slowly downhill	9	Pneumonia	+	No test
8	Subdiaphragmatic	Recovered	2	Perforated duodenal erosion	+	+
14	Subdiaphragmatic	Recovered	120	Sacrificed	+	+
15	Subdiaphragmatic	Recovered	15	Sacrificed	−	−
2	Subdiaphragmatic	Recovered	100	Sacrificed	+	+
26	Subdiaphragmatic	Recovered	86	*Intracranial hemorrhage following intraventricular injection	+	+

*These 2 cases represent the only such accidents in over 100 intraventricular injections on 15 monkeys

spasm described by Klee (1912 1910), Exner and Schwarzmann (1912 1914) as immediate on vagal section are purely temporary and probably due to irritation of the nerve section The retention is then probably due to early gastric paresis aided by reflex irritation of the remaining fibers Some investigators may have paid too little attention to normal variations in peristalsis and emptying time, and these may be considerable The period of postoperative examination has in many instances been too short, as Hughson (1925) has pointed out that any abdominal operation even a simple laparotomy delays the emptying of the stomach and this effect may persist for some time Koennecke (1922) however, who states that there is a definite delay in emptying carried out his investigations over a period of 11 months It appears clear therefore that the immediate effects of vagotomy splanchnicotomy and denervation of the stomach are similar, namely, retardation of function After a period, the peripheral (intrinsic) nervous mechanism assumes control of the denervated stomach and only one permanent symptom of importance i e , a decrease in initial emptying time, is observed

Meek and Herrin (1934) subjected 10 dogs to bilateral thoracic vagotomy and studied them for over 5 months by means of the fluoroscope, stomach pump, and forced (apomorphine) emesis The initial and final emptying times were carefully determined for several varieties of meal The nature of the meal was found to be all-important Vagotomy produced a permanent decrease in gastric "tonus" which greatly hampered the emptying of solids (including biscuit, milk curds, and precipitated barium) whereas it facilitated especially initially, the onward passage of fluids The accumulation of the delayed solid constituents ballooned the stomach and helped to increase the local tonus This coupled with a gradual postoperative hyperfunction of the peripheral mechanism kept the animals in excellent condition A contributory factor was the absence of satiety, due possibly to section of vagal afferents of a normal reflex that inhibits overfeeding They noted a transient period of dysphagia due to paresis of the lower esophagus without genuine cardiospasm

Our experience with vagotomized monkeys is seen to be in complete accord with this recent work, except with respect to cardiospasm

b Cardiospasm after vagotomy Our evidence from experiments with monkeys, clearly indicated a persistence of this phenomenon for many months after vagotomy, and may be interpreted along the following lines Vagotomy removes the extrinsic reflex mechanism for the *co-ordination* of esophageal and gastric movements and for the control of the relaxation of the cardia As we have repeatedly observed by catheter exploration and by X-rays, vagus stimulation by pilocarpine and large doses of acetyl-choline, causes cardiospasm (Fig 2a) by an action, presumably, on the parasympathetic motor (efferent) endings The locus of action is quite periph-

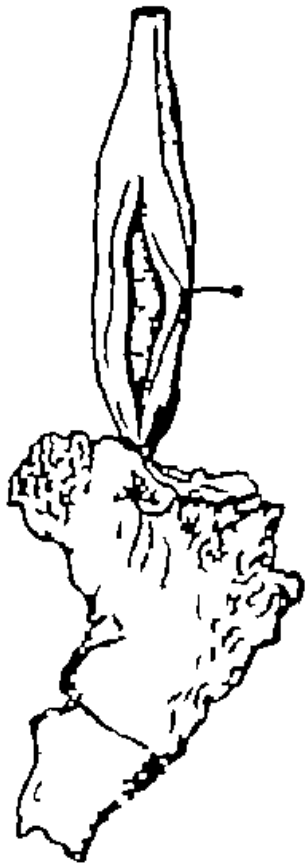

Fig 3 Green monkey N 12, dead of pneumonia on *ninth day after completion of bilateral neck vagotomy* Drawing of stomach (opened) and distended esophagus, demonstrating cardiospasm and food retention in gullet.

2 *Gastric motility* Although no planned investigation of the gastric motility had been undertaken in connection with these experiments, a number of observations have been collected which have a significant bearing upon this question. Apart from the animals with respiratory infections, all our monkeys ate ravenously after the operation and never seemed to be satisfied. It was only by means of a fluid diet and several days of fasting that the stomach could be sufficiently freed from food residues to permit of a satisfactory gastric analysis Indeed, lavage was usually necessary prior to the giving of the test meal The stomach was noticeably distended and relaxed in a number of the animals which came to autopsy While a certain amount of residual food material is a common finding in normal monkeys, examined postmortem, the picture in the vagotomized animal is striking. The residues are so bulky that they tend to form a cast as it were, of the interior of the stomach They are free from gross fluidity and obviously represent the more solid portions of the food such as cellulose, milk-curds, etc. and the individual components of dietary articles of as much as a week previously could often be identified Test meal samples could usually be obtained for nearly 2 hours as compared with the normal emptying time of 1 to 1½ hours Our scanty X ray data also afford evidence of gastric hypotonia and delayed emptying especially initial emptying These findings are exemplified in the roentgenogram (Fig 1b) and it may be emphasized that the barium meal in this case was highly viscid and a considerable portion of it had been injected into the stomach at the commencement of the observation. The roentgenogram taken after 40 minutes and fluoroscopic observation for 10 minutes longer failed to show any onward passage of the meal into the intestines Although we have insufficient data to specify the normal limits for the initial emptying time in monkeys, this animal on a previous occasion (before vagotomy) and two normal monkeys receiving the same barium meal on the present occasion, showed passage into the intestines within a few minutes We have noted delay of 15 to 20 minutes in one or two normal cases

3 *Discussion of vagotomy in relation to gastric motility* Esophageal dysfunction, gastric atonia, and pulmonary complications were noted by Rubaschow (1912) as the result of thoracic vagotomy in 16 experimental dogs Observations were made with the fluoroscope and also by means of a duodenal fistula.

4 *Gastric emptying after vagotomy* The literature on the effects of nerve section upon gastric motility is fully summarized in the excellent review by McSwiney (1931) who cites Cannon (1906 1911) Carlson (1913 1922) Nieden (1921) Koennecke (1922) Watanabe (1924) Stierlin (1920) Litthauer (1919) Litchenbelt (1912) and others, for data on vagotomized dogs, cats and rabbits The modern viewpoint on these rather conflicting data may be summarized in McSwiney's own words (p 493)

It is difficult to provide adequate reasons for this divergence of results The pyloro-spasm and cardio-

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2	Subdiaphragmatic	Recovered	160	Sacrificed	+	+
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eral, since these drugs, in our experience, increase the cardiospasm even in the vagotomized animal. After vagotomy the condition at the cardia is one of *achalasia* or removal of the co-ordinating reflex. The component of this reflex, which is important for the entry of food into the stomach is the phase of relaxation. After vagus section, therefore the cardia does not relax properly Whether there be a true spasm in addition to the failure to relax will depend on the state of the local muscular tonus and doubtless this varies from time to time and animal to animal The constancy and persistence of a true cardiospasm in monkeys suggests that this animal, in contrast to the dog and cat, has a high intrinsic tone of the cardio-esophageal musculature. The question arises may this be correlated with the known occurrence of striated muscle fibers in the lower esophagus of monkeys (and man)? We conclude that the adaptation of the mechanism of the cardia to the interruption of its normal vagal integration depends upon the *local* motility control. The smooth muscle wall of the cardia of the cat and dog may be expected to assume a peristaltic function although in the normal animal (McSwiney Alvarez) its contractions are "tonic" rather than "rhythmic The monkey's cardia, rich in striped muscle, is less able to develop rhythmicity and evinces a high grade of "tonus (postural" contraction) after vagal section. The fluidity of the food and the size and character of the boli swallowed play a correspondingly more important *rôle* in the overcoming of the handicap to the feeding mechanism in these animals

B Secretory disturbances (gastric) 1 Acidity In 18 examinations on the 6 vagotomized animals indicated in Table I (last column) there was never observed any diminution in the acid tide following a farina gruel test meal administered into the stomach via a tube. If anything, the acidity was rather increased after the bilateral vagotomy Observations have been made as early as the sixth day after vagotomy The unilateral operation was quite without demonstrable effect. The complication of food residues due to the stasis in gullet and stomach could be overcome by washing out with lukewarm water prior to the giving of the test meal, without materially influencing the results of the gastric analysis. In the animals surviving subdiaphragmatic vagotomy for long periods, a careful diet plus 36 to 48 hours starvation proved adequate preparation for the fractional gastric analysis

2 Mucus Evidence of adequate mucus secretion was obtained in all gastric samples from vagotomized animals *Bile* was rarely encountered

3 Vagotomy and the anacidity due to (intraventricular) pilocarpine or acetyl-β-methyl choline As reported previously (29) pilocarpine caused a complete abolition of gastric acidity (not affecting total chlorides) at the following threshold (per kilogram) doses, viz (1) 0 2 milligram via lateral cerebral ventricle, (2) 2.0 milligram intravenously and (3) 6.5 milligram subcutaneously After complete subdiaphragmatic vagotomy animal 21 failed to show the anacidity effect with intraventricular injections of pilocarpine in doses of 0.3 and 0.5 milligram per kilogram, but 1 0 and 1 5 milligrams doses gave the typical response. Animal 26 after vagotomy showed anacidity from intraventricular pilocarpine in doses of 0.5 milligram per kilogram (two occasions) Larger doses of pilocarpine were effective in producing gastric anacidity in vagotomized monkeys, Nos. 18 13 8 Before vagotomy animal 22 showed anacidity after an intraventricular injection of acetyl-β-methyl choline in a dose of 7 0 milligrams per kilogram. After the vagotomy 8 5 milligrams per kilogram were unable to abolish the gastric acidity but 10 0 and 12 5 milligrams succeeded These data suggest that any raising of the intraventricular threshold for the anacidity effect noted with parasympathomimetic drugs is slight, never reaching the intravenous threshold Vagotomy therefore, has lent no definite support to the possibility that the low intraventricular threshold for the anacidity effect might be due to a "central action" of the drug, and we are not prepared to subscribe to this explanation until more convincing evidence be adduced.

4. Discussion on the rôle of the vagi in gastric secretion. Hartzell (1930) using dogs and carefully controlling the psychic factor studied the (meat) test meal acidity for 6 weeks be-

fore, and 5 months after, operative vagus section Four animals with presumably complete severance of the intrathoracic vagi developed a marked lowering of gastric acidity One case, in which the posterior vagal trunk was missed, showed unaltered curves Two cases of subdiaphragmatic vagotomy (probably incomplete) gave variable results Vanzant (1931) found that 4 of Hartzell's dogs which survived bilateral vagotomy (including 3 of the intrathoracic route) ran an almost normal acidity after a year or two Shapiro and Berg (1932, 1934) found that even shorter times (4 to 6 weeks) sufficed for recovery to an approximately normal level of the acid secretion in a Pavlov pouch and in the gastric remnant after vagotomy combined with a subtotal gastrectomy Friedenwald and Feldman (1932), using an alcohol test meal and histamine stimulation on a series of 22 dogs, obtained little evidence of hypoacidity after a variety of partial vagotomies, but severance of the posterior (left) vagal trunk occasionally effected some hydrochloric acid lowering Thompson (1930) found that bilateral subphrenic vagotomy lowered the gastric secretion in the pylorectomized stomach of dogs, but attributed a major rôle to the neutralizing influences of food proteins and regurgitated bile De la Camp (1929) noticed that vagotomy did not abolish the histamine hyperacidity and tendency to peptic ulceration in experimental rats

Hartzell (*v supra*) reviewed the earlier literature The importance of the rôle of the vagus nerves in the regulation of gastric acidity came to be recognized in the latter part of the 19th century Hartzell cited Ducceschi (1917), Bircher (1920), Stierlin (1920), Borchers (1920), Latarjet (1922), Foa (1927), Dudek (1927), and Alvarez (1929) as obtaining experimental evidence (chiefly on dogs) that diminished gastric secretion could result from operative interference with the gastric vagal innervation, especially in conjunction with additional surgical procedures such as the Pavlov-Heidenhain pouch operation or partial gastrectomy

Physiologists distinguish several phases in the normal stimulation of the gastric secretion Pavlov (1910) discovered the initial (first phase) reflex (or psychic) secretion and believed it to be dependent upon the integrity of the vagi (the efferent path), a conclusion supported by Farrell (1928) Orbeli (1906) noted after vagotomy a marked reduction in the secretion of both acid and pepsin in Pavlov pouch dog fed *via* a gastric fistula He concluded that the reflex secretion continued from the stimulation due to the food in the stomach, even in the absence of a psychic factor The fact that some pouch secretion did occur in Orbeli's experiment suggested that a stimulating substance (hormone) is carried through the blood stream from the gastric remnant to the fundic pouch Edkins' *gastrin* (1906) was a secretogogue extract of the gastric (antral) mucosa and Popielski (1909) and others showed that a number of tissues can yield similar extracts Rasenkow (1925) recorded a stimulation of both hydrochloric acid and pepsin secretion in one dog after transfusion with the blood of another dog which had recently been fed Lim, Ivy, and their co-workers were unsuccessful in demonstrating this in a crossed circulation experiment Ivy and Farrell (1925) were able, however, to transplant a gastric (greater curvature) pouch into the (lactating) mammary gland This pouch was ultimately without its old blood and nerve supply, yet it gave a typical secretion (a) when food was ingested into the gastric remnant and (b) when the pouch itself was stimulated mechanically (balloon) or chemically (food) Klein and Arnheim (1932) successfully repeated this experiment and Klein (1932) further made pouches from the mucous membrane alone, without the muscular coats and plexus of Auerbach The same secretory powers were observed, and the high and constant level of the total chloride values were especially noted Carlson (1919, 1923) recorded that vagotomy failed to abolish the "continuous secretion" of the *resting* pouch or fistulous stomach of dog and man

Ivy and his co-workers have also studied a third or *intestinal phase* of gastric secretion The evidence all points, therefore, to a certain secretory function of the vagus which plays the dominant rôle in the initial or psychic phase of secretion but, once the food

has entered the stomach local and hormonal stimuli begin to play a more and more important part, the reflex (vagal) phenomena persisting in a subsidiary rôle.

Our own data on monkeys contribute evidence in favor of the view that the local (gastric and intestinal) phases of acid and chloride gastric secretion are well able to continue in spite of the operative severance of the vagus nerves.

GENERAL DISCUSSION

1 *Regulation of gastric acidity* Hickel (1925) reviewed the experimental data which point to the parietal (oxyntic) cell as the unit primarily concerned with the gastric hydrochloric acid secretion In a series of papers on the physicochemical aspects of gastric acidity Hollander Cowgill and Gilman (36 37 41–45) gave evidence that (1) the total chlorides of the gastric juice paralleled the concentration of electrolytes in the circulating blood and (2) the *maximum* free acidity obtainable in the pure gastric juice of dogs cats and humans was close to 150 milli-equivalents per liter (pH = 0 91 ± 0 02) which significantly approximated to isotonicity with the blood chlorides These data indicated that the oxyntic cells secrete "all-or-nothing" to maintain the ion equilibria between the gastric contents and the blood supply This is analogous to the rôle of the renal glomerulus in urine formation It conceives of each acid secreting cell pouring out hydrochloric acid (or its intermediary?) to meet an osmotic requirement It admits of individual cellular activity under (a) local control (metabolites, direct stimuli) and (b) hormonal influences acting via the blood stream, and perhaps, (c) secretory nerve impulses, but the primary controlling mechanism is the osmotic state of the blood relative to the gastric contents Although the classical description of the histology of the gastric mucosa emphasizes a preponderance of oxyntic cells in the fundic glands, they are by no means absent from the pyloric mucosa, as is evident from the observations of Shapiro and Berg (1934) that the total acidity in the pyloric remnant after subtotal gastrectomy was but little lower than that in a Pavlov pouch made at the time of the operation. Priestly and Mann (1932) also gave data to show that the pyloric mucosa can secrete an abundance of hydrochloric acid Shapiro and Berg's experiments also emphasize that a very small amount of acid secreting mucosa can elaborate a large quantity of acid, the implication being that the osmotic equilibration mentioned is complete under nearly all conditions Bernheim (1931) found that ligation of the gastric vessels either necrosed the stomach and killed the animal or more usually a collateral circulation quickly developed and permitted the continuation of a normally acid gastric secretion Variations in blood supply would seem, therefore, not to exert an appreciable influence on the attainment of the osmotic equilibrium Although these deductions are tentative, it would seem clear that the acidity is very difficult to influence by experimental procedures aimed at its fundamental mechanism There is no evidence to implicate the vasomotor nerves as a direct factor in the control of gastric acidity Vascular involvement in conditions of disturbed motility (e g , spasm) is a hypothetical and unlikely contingency The only established facts to date are that the gastric mucosa can secrete acid provided it has a blood supply and all conditions effective in stimulating gastric secretion involve an increased blood supply (Lim, Ivy and McCarthy) A direct secretogogue action of the vagi upon the acid secreting cells would seem likely from the occurrence of acidity in the gastric juice from a Pavlov but not from an Heidenhain (denervated) pouch in response to psychic stimuli (Pavlov Ivy) It is quite certain, however that the vagi are not an essential pathway for the secretory impulse since the vagotomized stomach or pouch secretes acid in response to histamine and local mechanical and chemical stimuli (v *supra*) The data thus tend to minimize the importance of vagal influences on the acid secretion and point to the circulation as the immediate controlling factor Perhaps some light may be shed upon the question by the study of the parallelism of histamine acidity and intragastric (or pouch) temperatures, used as an index of the circulatory activity by Thiessen and Snell (1933)

On the other hand, there is abundant evi-

dence that the "organic" secretions of the gastric mucosa are under the regulating influence of nervous factors, both excitatory and inhibitory (Pavlov, Babkin) We may refer particularly to the data secured by Babkin and his collaborators on the composition of the gastric juice from canine pouches under various experimental conditions Babkin and Komarov (1932) have stressed the importance of the *mucus* secretion In addition to "visible mucus" (from the surface epithelium) there is "dissolved mucus" which is secreted, in all probability (Babkin, Webster, Komarov), along with the pepsin from the "chief" cells of the gastric glands Mucus (free and dissolved) is able to neutralize a considerable degree of free acidity in the stomach, especially at the beginning and end of the secretory period, it also possesses antipeptic powers Babkin found that the composition of "mixed gastric juice" depended upon the type of stimulation by which it was called forth Thus (a) sham feeding (involving vagal stimulation) and (b) pilocarpine injections (small doses, subcutaneously) result in a juice which is rich not only in acid but also in pepsin and mucus, while (c) true feeding and, especially, (d) histamine injections give a highly acid juice poorer in organic constituents Two experimental complications must be ruled out, viz , (1) an irritant factor associated with inflammatory products from the mouth of the pouch or with the sampling apparatus, and (2) reflex factors associated with the peritoneal and other injury during the period of a few weeks after the pouch operation (ref Shapiro and Berg) After elimination of these technical difficulties, there remains good evidence that the organic part of the gastric juice is secreted as an alkaline, chloride-rich material best exemplified in the small volume of "continuous secretion" obtainable in the "resting phase" of the pouch

If a major rôle (Babkin) in the neutralization of the acidity of the parietal cell secretion can be ascribed to the alkalinizing effects of the organic secretions of the principal and mucoid cells, it is easy to explain any variation in the acid values of the "mixed juice," even from a gastric pouch where casual factors such as swallowed saliva, food, and regurgitated bile (Boldyreff, 12) may be completely ruled out Our data on monkeys are not free from the complications of these "casual factors" but, in an analysis, do afford evidence that the gastric neutralization mechanism can be extremely effective in these animals under certain experimental conditions Thus, pilocarpine (29) and acetyl-β-methyl choline (30) can produce a complete anacidity in from 5 to 10 minutes when given in sufficient dosage *via* intraventricular, intravenous, or subcutaneous routes The inability of vagotomy to alter significantly the intraventricular threshold for this effect, is interpreted as strong evidence against the entertaining possibility of a "central action" An alternative explanation, based on theoretical considerations, is tentatively advanced as follows Presuming the anacidity to result from a gastric neutralization mechanism (*v supra*), it will require a *continuous* secretion of sufficient alkalinizing material throughout the digestive period *Subcutaneous* administration of parasympathomimetic drugs directly stimulating the chief and mucoid cells, would require the largest dosage owing to the slow rate of absorption *via* this route *Intravenous* injection would be expected to get the drug to the peripheral locus (the gland cell) most quickly, but the rapidity of elimination and inactivation of the circulating poison would militate against a sufficiently prolonged action to be really effective The temporary effect of intravenous injections of acetyl-β-methyl choline was especially noted (Ferguson and Smith, op cit), although it was not strictly confined to this route of administration *Intraventricular* injection might be supposed to have the advantage of a moderately rapid absorption rate coupled with a *continuous absorption* over a long period[1] thus maintaining the effective neutralization of gastric acidity by the "organic secretion," with the minimum dosage An analogy is seen in the superiority of the intraperitoneal route for continuous absorption of glucose saline, and the barbiturate anesthetics, etc. The antagonizing action of atropine (again a

[1]The literature yields insufficient information as to the rate of absorption of dissolved substances *from* the cerebral ventricles, and we are at present engaged in a series of experiments by which we hope to throw light on this point.

peripheral action) is quite in accord with this explanation.

2 *Nerve supply of stomach and ulcer formation* Much experimental work has been done on the relation of peptic ulcer to the neuro-motor and neuro-secretory mechanisms of the stomach, and a full account of the rather conflicting literature appears in the articles by Greggio (1916) McCann (1929) Cushing (1932) and Best and Orator (1932) The rabbit has usually been employed which is unfortunate as this animal may show gastric lesions after a wide variety of experimental procedures and because it is prone to serious sequelæ from vagotomy or splanchnicotomy (Alvarez, 1929) Dogs were used by Latzel (1913) in a series which included 10 cases of hemorrhagic erosions and ulcerations following subdiaphragmatic vagotomy The following conclusions may be drawn from a survey of the literature (1) hemorrhagic lesions and acute erosions (sometimes perforating) are much easier to produce than true (chronic) peptic ulcers, indicating that the underlying pathology is far from simple but must embrace a number of varying factors (2) vagotomy (bilateral) is likely to be followed by such lesions, but splanchnicotomy and also adrenalectomy (72 91) are probably even more effective in producing erosions the incidence of lesions varies greatly in the different records (3) Irritation of the vagi may be a factor (Singer 1928 Stahnke, 1924 Keppich 1921 Lorenz, 1916 dalla Vedova, 1900 *et al.*) (4) Okkels' (1927) suggestion that pathological changes in the vagus nerves, or in the vagal nuclei (Singer 1928) may dispose to ulcer chronicity is not supported by experimental evidence (Best and Orator 1932)

While the extent to which the central nervous system is implicated in the ulcer problem (McCann 1929 Cushing 1932) is beyond the scope of the present discussion it may be noted that the experience of Fulton and associates in the Yale laboratory suggests a significant incidence of alimentary lesions in monkeys with experimental injury to the hypothalamus, confirming Cushing's human data and those of Keller (1933) on dogs

No discussion of the pharmacological approach (Westphal, 1913 Friedman 1918 Underhill and Freiheit, 1918 Light, Bishop, and Kendall 1932) will be attempted beyond noting that we have given 15 monkeys over a hundred intraventricular injections of pilocarpine in doses from 0.15 to 1, 1 milligram per kilogram without the slightest evidence of gastric or intestinal lesions that could be related to these injections We have, on occasion even administered dilute hydrochloric acid to counteract the anacidity noted in these experiments One animal, only showed a small peptic ulcer on the lesser curvature at the end of one of several linear abrasions caused by the previous passage of a hard stomach tube. In life this animal showed hyperacidity barely affected by massive doses of pilocarpine (29)

3 *Applications to the surgery of peptic ulcer* Clinical experience has amply demonstrated the need for control of the gastric acidity as an integral part of the treatment of peptic ulcer Our experiments on monkeys show that vagotomy may be followed by gastric lesions (albeit rarely) The procedure is ineffective in controlling the gastric acidity of these animals. Our earlier data proved the ability of parasympathomimetic drugs, suitably administered to abolish the normal gastric acidity although failure was recorded with one case that developed a traumatic ulcer Apart from the strong condemnation of these drugs on account of their unpleasant side-reactions, they would not be suggested for clinical use in the light of the previous discussion. Vagotomy and subtotal gastrectomy proved unreliable are also to be censured for the same scientific reasons Actual" gastric acidity represents the admixture of the hydrochloric acid secretion of the parietal cells with the alkalinizing secretions of mucus and pepsin Experimental attempts to abolish acidity by lessening acid secretion are bound to fail, because the oxyntic cells, if they function at all will secrete maximally (as determined by simple osmotic considerations) and their activity is not modifiable by nerve section mucosal removal and vascular changes The practical control of gastric acidity is, therefore, largely a matter of simple neutralization With vagotomy and gastrectomy complicated neutralizing factors may be in

troduced (1) disturbed balance of secretions (2) unexplained postoperative hypo-acidity, (3) alkalinizing inflammatory materials in stomach remnant (postoperative), (4) regurgitation of bile (largely discredited)

In conclusion, therefore, it may be argued that, in so far as they aim to modify gastric acidity and motility and so alleviate the symptoms rather than strike at the cause (still, regrettably obscure) of ulcer, surgical procedures are open to the criticism that they interfere more or less seriously with the normal physiological functions of the stomach Both the movements of the organ and the acidity of its secretions are amenable to a certain degree of control by medical measures such as rest, diet, alkalies, "mucin" (Brown, *et al*), drugs, and so on There are definite indications for surgical interference, e g, hemorrhage, perforation, obstruction, or danger of neoplasm *Gastro-enterostomy* has been proved effective in neutralizing the gastric acidity by a reflux of alkaline bile A number of surgical details must be followed in order for this operation to achieve the purposes for which it is intended, viz, (a) relief of obstruction, (b) regurgitation of bile into the stomach It may fail in certain cases and in others be followed by complications such as ulceration of the site of anastomosis, etc. Nevertheless, this type of operation has been much used where conservative measures have failed or where economic and occupational reasons militate against effective non-surgical treatment It is thoroughly rational in the light of the foregoing physiological discussion Whether the same can be said for the more radical surgery of denervation and subtotal gastrectomy (particularly in the absence of the cited "major" indications) may be discussed not only from the clinical viewpoint but also from the standpoint of the conclusions reached in the review which we have presented concerning the underlying mechanisms for the control of the stomach functions

SUMMARY

Complete operative severance of the vagus nerves of the green monkey (in the neck, 5 cases, subdiaphragmatic, 5 cases) resulted in the following sequelæ

1 Cardiospasm, of a persistent type, occurred in all cases, there was evidence of gastric hypotonia and of delay in the onward passage of *solid* foodstuffs

2 The acid tide following a test meal was not lowered in the 6 animals subjected to fractional gastric analysis

3 Only a slight rise occurred in the intraventricular threshold for the anacidity effect previously found as a typical response to injections of the parasympathomimetic drugs, pilocarpine and acetyl-β-methyl choline (hydrochlorides)

4 Two animals showed mucosal erosions at autopsy, one case in the stomach and the other in the duodenum, the latter leading to the death of the animal

The possible rôle of the vagi in (a) peptic ulcer, (b) gastric motility, and (c) the secretion of the gastric juice, is discussed Consideration is also given to the application of the physiological data to an evaluation of the rationale of gastric surgery

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EFFECT OF TOTAL HYSTERECTOMY UPON THE OVARY OF THE MACACUS RHESUS

An Experimental Study[1]

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THE uterus, that venerable organ which in one mood provides mankind with its first shelter, and in yet another subjects woman to a great proportion of her woes, is unique again with respect to its position in the realm of female sex hormonology Stimulating no little investigation as to its part in the complex interplay of reproductive autocoids, and mirroring so acutely the effects of these cryptorhetic influences, it has as yet been assigned no definite rôle other than that of ancillary passivity, dominated and coerced, through the ovary, by that glandular autocrat, the anterior pituitary Definitive evidence indicating an endocrine contribution on the part of the uterus would doubtless be as gratifying to the harassed clinician attempting to explain away an early post-hysterectomy menopause as it would prove stimulating to the endocrinologist

The present experiments have been an attempt to shed some light on the subject from the experimental standpoint

LITERATURE

Studies on the human ovary after hysterectomy are conspicuous largely for their lack of evidence Werth (1902) described an increase in the size of the follicles with a conspicuous absence of follicular ova in human ovaries following hysterectomy, while Keitler (1904) observed what he considered a significant diminution in the number of follicles after excision of the uterus Jacobsohn (1914) likewise reported fewer follicles present in the ovaries of hysterectomized women

Vineberg (1915) and Hawks (1921) have described cystic ovaries found at a second operation following hysterectomy

Lindig (1922) noted follicular enlargement following the removal of the uterus in women, while Terada (1921), in an experimental study, observed follicular atresia in the ovaries following hysterectomy Schubert (1930) was able to find no ova after uterine excision

Regardless of the discrepancies in the reported condition of the ovary after hysterectomy, there is general agreement among clinicians that removal of the uterus does hasten menopausal symptoms

Sessums and Murphy (1932), in an analysis of 91 cases of hysterectomy with complete or partial conservation of ovarian tissue in women below 36 years of age, report the appearance of unmistakable subjective menopausal symptoms in 43 per cent before the age of 40 years

Attempts to adduce evidence of the influence of the uterus on the ovaries from the purely experimental standpoint has been but little more convincing

Marshall (1922) states that the ovary of the rabbit is found normal 10 months after removal of the uterus, and that hysterectomized females accept the male Long and Evans (1922) could detect no effect from hysterectomy on estrus in the white rat Hartman (1925) states that hysterectomy has no effect on the cycle in the opossum

Removal of the uterus has no effect on the voluntary activity of the white rat as shown by Durant (1927), and Deanesley and Parkes (1933) have reported that hysterectomy is without effect on the estrous cycle of the ferret

Siegmund (1933) found that the ovaries of young female dogs do not lose their ovulatory activity after hysterectomy, but cites the work of Zimmerman who found that hysterectomy in young bitches was followed by marked histological changes in the ovaries, characterized by disintegration of the eggs, formation of cystic follicles, follicular hematoma, and the absence of corpora lutea

Probably the best substantiated evidence indicating that hysterectomy influences the

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ovarian cycle is the work of Leo Loeb (1927) who showed that hysterectomy following ovulation in the guinea pig results in persistence of the corpus luteum. More recently Asdell and Hammond (1933) have found that *removal of the uterus in the rabbit is followed* by prolongation of the life of the corpus luteum, and that this persistence of the corpus luteum is not merely of one form, but of partial function as well since postcopulatory ovulation does not occur in these animals. The period of corpus luteum persistence is, however much shorter in the rabbit than in *the guinea pig.*

Seesums and Murphy (1933) in a series of experiments on rabbits state that hysterectomy in these animals tended to inhibit estrus and produced degenerative and inhibitory changes in the ovaries. These workers believe that endometrial autotransplants limit these inhibitory and degenerative changes and con*clude that the endometrium probably elaborates* a hormone which influences the ovary

Murphy (1934) failed to find any changes in the weight of the ovaries in the white rat following uterine excision.

Mavromati (1932) found that hysterectomy in rats was followed by prolonged estrus and that rats in which prolonged estrus occurred *spontaneously showed atrophic uteri at au*topsy This worker felt that these results indicated that the uterus either destroys large amounts of theelin or inhibits its formation, and that with the withdrawal of this influence the excess of theelin continues to keep the vaginal epithelium in a stage of active estrus Such a view seems scarcely tenable when one reflects that he used but 8 animals and does not mention such control conditions as diet and environment.

EXPERIMENTAL

Five female Macacus rhesus monkeys were used. Two of these were mature, having definite menstrual records and showing recent *corpora at the time of operation* The 3 remaining were immature, as evidenced by size, history of no menstruation, immature type of sex skin [1] and the absence of large *follicles or corpora* at operation. Total supravaginal hysterectomy and total bilateral salpingectomy was carried out in each animal. *Ovaries* from 4 animals 2 mature and 2 immature, were studied for controls

Operative procedure The animals were anesthetized with ether and catheterized The abdomen was shaved, prepared with iodine and alcohol, and draped with a sterile laparotomy sheet. A midline incision was made from just above the symphysis to a point 1 centimeter below the umbilicus. The peritoneum was carefully opened and the presenting viscera carefully packed away with gauze strips moistened in warm, sterile saline. The uterus was then picked up and measured at the level of the uterine horns The ovaries were also measured care being used not to injure them. The tubes were dissected free from the ovaries, meticulous precautions being taken not to disturb the ovarian blood supply The broad ligament was divided between the abdominal wall and the uterus, division being carried to the point at which the peritoneum is reflected posteriorly over the rectum and anteriorly over the bladder

At this point the uterus was elevated by means of an Allis clamp and the peritoneum stripped from the lower segment, the peritoneum being *reflected backward and downward.* The vagina was clamped off just below the cervix by means of a Kelly clamp and the uterus and cervix were removed. After carbolization, the stump was closed with a purse-string suture and the peritoneum was brought together and closed over the stump After it had been determined that no bleeding was occurring the ovaries were carefully isolated from the surrounding viscera and the abdomen was closed by means of four rows of sutures A collodion dressing was applied to the outer wound

Following operation the monkeys were observed daily for color changes in the sex skin," and vaginal lavages were done every second day The animals were explored at intervals and measurements made of the ovaries as well as observations for large *follicles and corpora lutea.* At these times, care was taken in no wise to traumatize the ovaries

[1] The sexual skin, or genital skin, refers to the reddening and swelling about the genitalia. The term "sexual skin" was first applied by Longley and Shoemaker (1931)

Vaginal lavage technique The method used was that described by Hartman (1932) A uniform quantity of 2 cubic centimeters of physiological saline was used to make each lavage, the fluid being withdrawn and reinjected into the vagina three times One cubic centimeter was withdrawn and placed in a vial and the sediment allowed to settle over a period of 12 to 18 hours The amount of sediment was read at the end of this time by means of a scale

Lavages were made on the average of three times per week`

At the end of the experiment, the animals were sacrificed and the ovaries removed and studied from serial microscopical sections The number of normal, atretic, and polyovular follicles was counted and recorded in each case Microscopical studies of the excised uteri and tubes were made, particular care being taken to obtain sections through the entire lower portion of the cervix at the line of amputation

The pituitary glands were removed at autopsy and submitted to another investigator for later cytological studies

OBSERVATIONS

From the amount of sediment in the vaginal lavage it was possible to determine the time at which a recent corpus luteum could be expected This was confirmed in three instances by operation The time interval between the points of highest sediment content was fairly constant for the individual animal

Histological sections of the excised uteri showed that amputation of the cervix had been complete in every instance

The condition of the ovaries from the time of hysterectomy until the termination of the experiment is recorded in the protocols

A census of normal and atretic follicles found in the ovaries of the experimental animals is given, together with a census of control ovaries, in Table I

Daily color records of the "sex skin" of the hysterectomized series showed no variation from the normal Throughout the experiment the animals remained among the healthiest in the colony, and all showed consistent monthly weight gains

PROTOCOLS

Monkey 21 This animal was considered before operation to be sexually immature because of the absence of menstruation and the pale color of the sex skin This was confirmed at operation

July 19, 1934 The uterus and both tubes removed The right ovary measured 9 by 7 by 5 millimeters, left ovary 10 by 7 by 6 millimeters No corpora were present, although both ovaries contained several follicles 1 millimeter in diameter

September 7, 1934 Fifty days after hysterectomy, a laparotomy was performed Dense adhesions were encountered Both ovaries were firmly bound down The right ovary measured 9 by 6 by 12 millimeters, left ovary 9 by 5 5 by 4 5 millimeters No corpora or large follicles were observed

October 31, 1934 Fifty-three days after the first laparotomy, and 103 days after hysterectomy, the animal was again explored Abdominal adhesions were more marked than on the previous exploration, but the ovaries were no closer bound down than before The right ovary measured 11 by 9 5 by 10 millimeters, left ovary 10 5 by 8 5 by 8 millimeters The left ovary contained a recent corpus luteum and several well developed superficial follicles The right ovary contained an old corpus luteum and several very small superficial follicles

February 20, 1935 Two-hundred and sixteen days after hysterectomy the animal was sacrificed Both ovaries were surrounded by rather dense adhesions The right ovary measured 8 by 8 by 7 millimeters, left ovary 7 by 6 by 5 millimeters No corpora were present

High vaginal sediment levels occurred at 22, 23, 25, 26, 21, and 22 day intervals, in the order given

Monkey 37 This animal was also thought to be, and later proved by operation to be, sexually immature.

August 6, 1934 A total hysterectomy and bilateral salpingectomy were carried out The right ovary measured 11 by 5 by 9 millimeters, left ovary 12 by 6 by 11 millimeters No corpora or large follicles were found

October 29, 1934 Fifty-four days after hysterectomy, an exploratory laparotomy was performed and the ovaries measured When the peritoneum was opened a formidable mass of adhesions was encountered Both ovaries were completely swathed in dense fibrous adhesions and were freed with considerable difficulty The right ovary measured 8 by 5 by 7 millimeters, left ovary 7 by 5 by 6 millimeters No corpora or large follicles were found

January 3, 1935 Ninety-six days after the first exploratory laparotomy and 150 days after hysterectomy, the abdomen was again opened The ovaries were carefully freed from the surrounding adhesions and removed The right ovary measured 12 by 9 by 8 millimeters, left ovary 10 by 9 by 8 millimeters No corpora or large follicles were present The blood supply to both ovaries was good The high levels of vaginal sediment were found at 20, 16, 23, 20, and 18 day intervals

Monkey 40 This animal had never menstruated, and this fact, together with the pale color of the sex skin led us to classify the animal before operation as sexually immature This impression was confirmed at operation.

July 25 1934 The uterus and tubes were removed The right ovary measured 9 by 5 by 5 millimeters and the left ovary 8 by 6 by 5 millimeters. No corpora or large follicles were present

October 9, 1934 *Seventy-six days after hysterectomy* the animal was explored and the ovaries measured right ovary 10 by 7 by 6 millimeters, left ovary 8 by 6 by 5 millimeters No corpora or large follicles were found Firm, dense adhesions were *found surrounding both ovaries*

November 23 1934 Forty-five days after laparotomy and 121 days after hysterectomy the animal was killed and the ovaries measured right ovary 8 5 by 6 by 5 millimeters left ovary 8 5 by 6 5 by 7 millimeters. *No corpora or large superficial follicles* could be seen.

Vaginal lavages showed the greatest amount of sediment present at 30, 31 and 29 day intervals, in the order given

Monkey 60. This animal was mature and menstruated regularly

July 26, 1934. Total hysterectomy and bilateral salpingectomy were performed The right ovary measured 11 by 9 by 7 millimeters, and the left ovary 9 by 7 by 6 millimeters. The right ovary contained one recent corpus luteum.

September 25, 1934 Sixty days after hysterectomy a laparotomy was performed and the ovaries examined The right ovary measured 7 by 8 by 5 millimeters the left ovary 9 by 6 by 8 millimeters and contained one large follicle. No corpora were present in either ovary

November 11 1934 Forty-seven days after laparotomy or 107 days after hysterectomy the animal was again explored. (Note the left ovary was free in the abdominal space the right was bound down by adhesions) The right ovary measured 7 by 7 by 7 millimeters while the left measured 10 5 by 10 by 9 millimeters. There were no large superficial follicles in either ovary The left ovary contained an old corpus luteum estimated as about 1 month old

February 27 1935 One hundred and ten days after the second laparotomy and 217 days after hysterectomy the animal was sacrificed The right *ovary measured 10 by 9 by 7 millimeters* the left, 11 by 7 by 6 millimeters No corpora or large superficial follicles were found

The greatest amount of sediment by vaginal lavages occurred at 27 27, 31 22 and 19 day intervals

Monkey 93 This animal was a large, mature female with a definite menstrual history Operation was performed July 25 1934, and the uterus and tubes were removed The measurements of the ovaries at this time were right ovary 12 by 11 by 9 5 millimeters left ovary 9 by 8 5 by 7 5 millimeters There was present one recent corpus luteum in the right ovary and one large follicle in each ovary (3 millimeters in diameter) The uterus was very vascular and the tubes markedly hyperemic.

September 21 1934 Sixty days after hysterectomy a laparotomy was performed to ascertain the condition of the ovaries Extensive adhesions were encountered, and some difficulty was experienced in locating the left ovary The right ovary measured 8 by 6 5 by 6 millimeters and the left ovary was *found to be 11 by 10 by 10 millimeters.* No corpora were present in either ovary but a large follicle was present in the left ovary

December 3 1934 Seventy-three days after laparotomy and 133 days after hysterectomy the animal was sacrificed and the ovaries were examined grossly The ovarian measurements were right ovary 10 by 9 by 8 millimeters left ovary 9 by 8 by 7 millimeters No corpora or large follicles were present in either ovary

By vaginal lavage the highest sediment levels appeared at 30, 17 30, 25 and 25 day intervals, in the order mentioned.

EVALUATION OF STUDY

The literature concerning the effect of hysterectomy upon the ovaries is far from being in agreement Clinical observers are unanimous in their opinions that the removal of the uterus is in many cases followed by the premature appearance of subjective menopausal phenomena Interpreted as indicating functional impairment of the ovaries. Concerning the appearance of the ovaries themselves, there is less agreement as to the type and degree of structural change found, but all observers report changes of one sort or another

Experimental studies, while obviously incapable of contributing anything toward the subjective elements in the problem, tend to demonstrate for the most part that the removal of the uterus is without any marked effect upon the ovaries in the several species studied The work of Loeb (1927) demonstrating persistent corpora up to 90 days after hysterectomy following ovulation, the studies of Asdell and Hammond (1933) indicating a similar persistence of the corpus luteum in the rabbit and the findings of Seesams and Murphy (1933) indicating that hysterectomy in the rabbit is followed by degenerative changes in the ovary and that endometrial implants prevent the appearance of these changes, are the most suggestive and certainly the best authenticated of the work indicating

that hysterectomy does influence the ovary However, it must be borne in mind that the rabbit is in many respects a notoriously capricious experimental animal The significance of the work of Loeb and of Asdell and Hammond is not clear as yet

Regardless of the histological variations that can be demonstrated in the ovaries of hysterectomized animals, the final proof of ovarian activity, or inactivity, must come from an investigation into the functional aspect of that organ Fortunately, the ovary lends itself admirably to such a study The maturation of ova, the development of follicles, and the formation of corpora lutea are all "anatomical footprints" left in the wake of physiological transpirations, and by them we are enabled to trace sequentially, as it were, the trail of functional events through that organ The finding of corpora is *prima facie* evidence that the ovary is performing its normal function, viz that of ovulating, and the periodic examination of the ovary, together with a comparison of what we accept as the normal, enables us to detect variations in the rhythm as well as other changes

The Macacus rhesus, like the female of the human species, runs a regular menstrual cycle with this exception—the summer months are normally anovulatory The cycle averages 28 days (Hartman, 1932), and ovulation occurs normally from the tenth to sixteenth day after the onset of the last menstrual period, the average being on the thirteenth or fourteenth days (ibid)

The "sexual skin" of the female Macacus rhesus undergoes periodic fluctuations in color intensity during the cycle Throughout the follicular phase of the cycle there is a gradual increase in color up to a maximum, which is reached during the third week after the onset of menstruation This is followed by a gradual subsidence of color intensity until just after menstruation, when, with the development of new follicles, the color again begins to increase This has proved, in our experience, to be a valuable index of ovarian activity, for this coloring can be induced in ovariectomized monkeys by injections of ovarian follicular hormone (Collings, 1926, Allen, 1927)

Two questions present themselves in a study of this sort (1) Does hysterectomy prevent the development of sexual maturity in the immature female monkey? (2) Does removal of the uterus influence the ovarian cycle of the sexually mature monkey? If either, or both, of these queries are answered in the affirmative, then the mechanism of that influence must be inquired into Postulating for the sake of argument that excision of the uterus does influence the ovary, then two possible explanations present themselves First, that the effect of hysterectomy on the ovary is a purely traumatic one, the damage to the vascular or nerve supply to the organ producing trophic changes Second, that this disturbance is due to an endocrine relationship, as suggested by Sessums and Murphy (1933) for the rabbit

An analysis of the protocols reveals that of the three immature females, one, No 21, definitely went on to sexual maturity, as evidenced by the finding of a corpus luteum at laparotomy 103 days after removal of the uterus

The 2 other animals in the immature group did not reach sexual maturity, as shown by the consistent lack of corpora or large follicles in the ovaries Both these animals were smaller than monkey No 21, and it is our opinion that these animals would have developed into sexual maturity if sufficient time had been allowed before sacrificing the animals It should be mentioned that there was no significant reduction in the size of the ovaries and no changes could be detected grossly

Of the mature group, monkey No 60 gave clear cut evidence of ovulatory activity at laparotomy Monkey No 93 showed one large follicle ready to rupture at laparotomy 60 days after hysterectomy

A consideration of the census of follicles found in the ovaries at the completion of the experiment (Table I), compared to ovaries from the control group, reveals no significant differences

The percentage of follicles with antra was about the same for both the experimental and the control groups There was a comparable amount of follicular atresia in the experi-

TABLE I—INCIDENCE OF NORMAL AND ATRETIC FOLLICLES IN OVARIES OF HYSTERECTOMIZED MONKEYS COMPARED TO NORMAL

Monkey No	Ovary	Types of follicles				Polyovular	Percentage of atretic follicles
		Atretic		Normal			
		Small	Large	Small	Large		
				Experimental			
13—Immature	Right	76	3	230	77		24.7
93—Mature	Left	66	14	3	4		89
90—Immature	Right	76	10	30	17	4	39
60—Mature	Right	76	30	736	36		11
37—Immature	Left	88	11	231	39	10	31
				Control			
33—Mature	Left	28	13	160	66		30
47—Immature	Left	114	44	483	47	3	17
35—Mature	Left	64	18	204	34		17
14—Immature	Right	30	30	75	39	4	23

mental and control immature animals, but considerable variation was found in the percentage of atresia in the mature groups. This latter fact, however is to be expected since animal No 93 had recently ovulated, the ovaries from monkeys Nos. 33 and 35 were removed in the middle of the cycle, and since monkey No 60 had shown a high sediment level in the vaginal lavage 10 days before operation. Certainly there was no evidence of increased follicular atresia in either the mature or immature animals upon which hysterectomy had been performed.

It will be noted that frequent mention is made in the protocols of the rather dense fibrous adhesions found surrounding the ovaries It seems of no little significance to the writers that although adhesions were marked on superficial examination in every instance yet in only one animal (No. 93) were the ovaries completely encompassed by adhesions. In each of the remaining eight ovaries a considerable portion of the surfaces of the ovaries were free and closer scrutiny revealed the ovary lying for the most part in a small peritoneal pocket. It is interesting to speculate upon the relation of the intact capsular epithelium of the ovary to its retention of normal function.

SUMMARY AND CONCLUSIONS

Five female monkeys (Macacus rhesus) including mature and immature animals, were totally hysterectomized and the effect on the ovaries studied. The animals were followed for periods ranging from 121 to 217 days after hysterectomy No impairment of ovarian activity could be detected by vaginal lavage studies, sex skin" color records, or examination of the ovaries at laparotomy A postmortem census of the follicles in the ovaries revealed no increase in follicular atresia for either the mature or immature group One immature animal went on to definite sexual maturity 103 days after hysterectomy It is concluded that hysterectomy in the Macacus rhesus is without effect upon the ovary except for purely traumatic effects The monkey affords no evidence that the uterus contributes any endocrine influence upon the ovary

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THE ANOMALOUS RIGHT SUBCLAVIAN ARTERY

Its Practical Significance with a Report of Three Cases[1]

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IRREGULARITIES in the development of the major branches of the aortic arch are numerous indeed, and have been conveniently classified by Poynter (1916) as follows: (a) branches fewer than normal, as in the occurrence of bi-innominate arteries; (b) *branches more numerous than normal, as in* the absence of the innominate, and consequent separate origin of both carotid and subclavian arteries; (c) branches in abnormal succession, dependent upon an irregular development of the aortic-arch plan. The cases which we shall report belong to this last named group. *In them the right subclavian arises not* first, or in conjunction with the carotid of the same side, but as the last direct branch of the aortic arch (Figs. 1 and 5, 6 and 7). They are not uncommon, occurring in 1 in 120 cases.[2]

Our 3 cases of anomalous right subclavian *artery were encountered in the course of* routine laboratory dissection of 102 specimens[3] since they are essentially similar, one will serve as basis for description.[4] The first branch of the arch of the aorta was the right common carotid artery; it was followed in succession by the left common carotid, left subclavian, and (anomalous) right subclavian, all arising separately from the arch in the order named, from before backward. The first three branches in specimen I (Figs. 1 and 2) were placed at their origin, in almost parasagittal plane; in specimens II (Fig.) and III the first branch lay appreciably to the right of the succeeding two. In the 3 cases the two anterior trunks arose very close together; the second was separated from the *third by a slight interval*; between the latter and the anomalous vessel a greater one occurred, in which the esophagus lay. The anomalous subclavian artery in the 3 cases originated from the aorta at the level of the midportion of the third thoracic vertebra.[5] It ascended dorsal to the esophagus, to attain *the right side of the vertebral column opposite* the first thoracic vertebra. The right recurrent laryngeal nerve arose from the trunk of the vagus opposite the cricoid cartilage (Figs. 1 and 5).

The arrangement of aortic trunks and their visceral relations are dependent upon the *aberrant development of the aortic arch system* in the embryo.

Usually, as has been described with admirable completeness by Congdon (1922), the transformation of the aortic arch system involves the interruption of the right dorsal aorta (right fourth aortic arch) caudal to the origin of the primordial right subclavian artery (Fig. 3, at asterisk), so that the subclavian *arises either separately as the first branch* of the arch, or in conjunction with the right common carotid, through the innominate as intermediary. But in the type of anomalous origin represented in our specimens, the interruption occurs at a higher level, cephalad to the origin of the right subclavian (Fig. 4, at asterisk) so that the latter vessel then arises from the hinder part of the arch, just beyond the origin of the left subclavian artery.[6] This caudal segment of the right dorsal aorta, now incorporated into the right subclavian artery instead of becoming obliterated, is dorsally placed, and, as the body of embryo is already established, in the characteristic retro-esophageal location. Since the fourth right

[1] An attendance reported by Cawley (1917) in [illegible] [illegible] (Thompson) reports [illegible] per cent, Harvey [illegible] 8 per cent, Hochstetter 4 per cent. Since the publication of Cawley's results at least [illegible] observers of them in the [illegible] have been reported in the literature [illegible] Anderson (1917), Kirch (1917) [illegible] (1918), Gebele [illegible], Fromm [illegible], Spanchakow (1920), De Garis (1921), Punch Brentano (1922), Wood et al. (1924), [illegible] by Dalgaard (1924).

[2] [illegible] specimens during the winter quarter of 1924-5 [illegible] 68 during the autumn and [illegible] quarter of 1924-25, [illegible] examined in our laboratory since that reported by [illegible] (1918), making total of [illegible] specimens. No other aortic arch anomalies were found during the 8 years.

[3] They may be [illegible] for designated specimens I, II, and III. The relevant anatomy of specimen I is illustrated in Figures 1, [illegible] and 5; that of specimen II in Figures 6 and [illegible]; specimens III is not represented in the illustrations. Specimen I, white male, aged [illegible] years, height [illegible] feet 8 inches, weight [illegible] pounds; specimen II, white male, aged [illegible] years, height [illegible] feet 9 inches, weight [illegible] pounds; specimen III, black female, aged [illegible] years, height 5 feet 7 inches, weight [illegible] pounds. In specimen I the branches of the anomalous right subclavian artery were [illegible] in vertebral, superior intercostal (the second of [illegible]), deep cervical, internal mammary, [illegible] (the rest of transverse scapular). In specimens II and III, no record of the subclavian branches were available.

[4] According to Poynter (1916) and Cawley (1917), who have given full very comprehensive [illegible] of all aortic arch anomalies.

(Contribution No. [illegible] from the Anatomical Laboratory of Northwestern University Medical School.

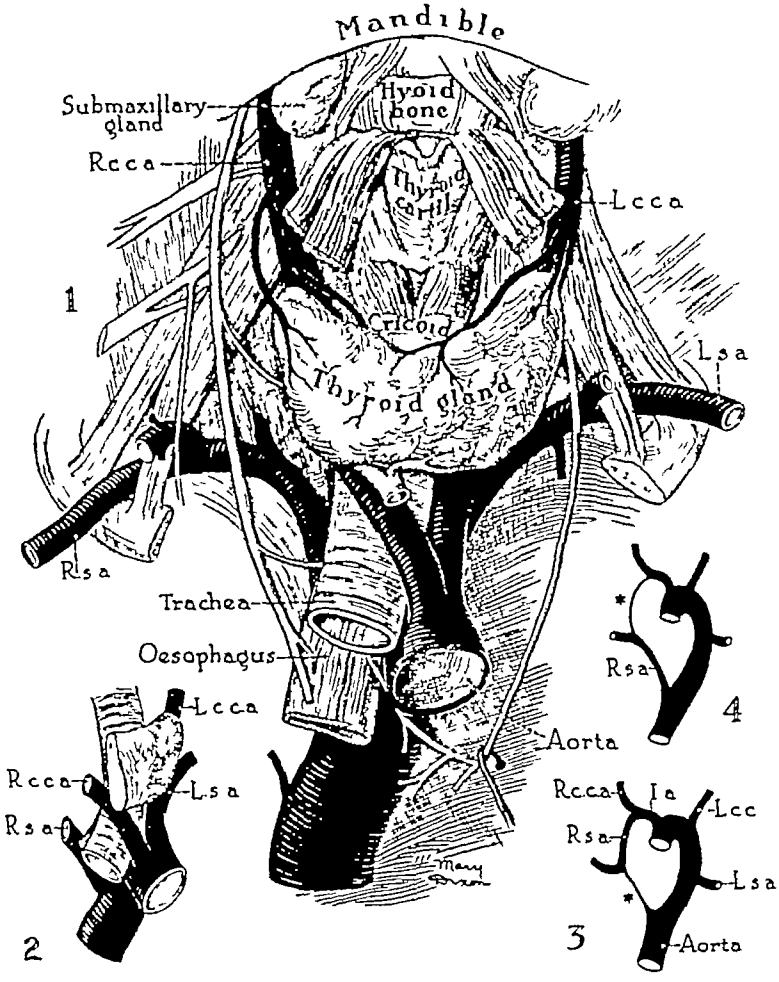

Fig 1 The deep structures of the neck and upper portion of the thoracic mediastinum in ventral view (specimen I) The platysma and sternocleidomastoid muscles, the cervical fascia superficial vessels and nerves, and deep veins have been removed to expose the great arteries arising from the aortic arch, the sternohyoid and omohyoid muscles have been cut Showing the location of the anomalous right subclavian artery, dorsal to the esophagus, and the retrothyroid position of the right common carotid artery (cf Fig 4) *Lcca*, Left common carotid artery, *Lsa* left subclavian, *Rcca*, right subclavian artery × 44 natural size

Fig 2 A portion of the area illustrated in Figure 1 showing the right common carotid and anomalous right subclavian arteries with their chief visceral relations as revealed by removal of the right lobe of the thyroid gland (cf Fig 1) Note, on the right side, the ventrodorsal succession of thyroid gland, common carotid artery, trachea, esophagus, anomalous subclavian artery × 22

Fig 3 Diagram of the aortic arch system in the 18 millimeter human embryo, showing the formation of the usual arrangement of branches from the arch (after Congdon, Figs 14, 15) Asterisk marks the short caudal segment of the right aortic arch which will disappear, the cranial segment will become the right subclavian branch of the innominate artery (as in Fig 8, normal adult arrangement) *Ia*, innominate artery, other abbreviations as before × 22

Fig 4. Diagram to show the formation of the anomalous right subclavian artery (labeled) as the last branch of the aortic arch, the segment between common carotid and subclavian disappears, there is no innominate artery

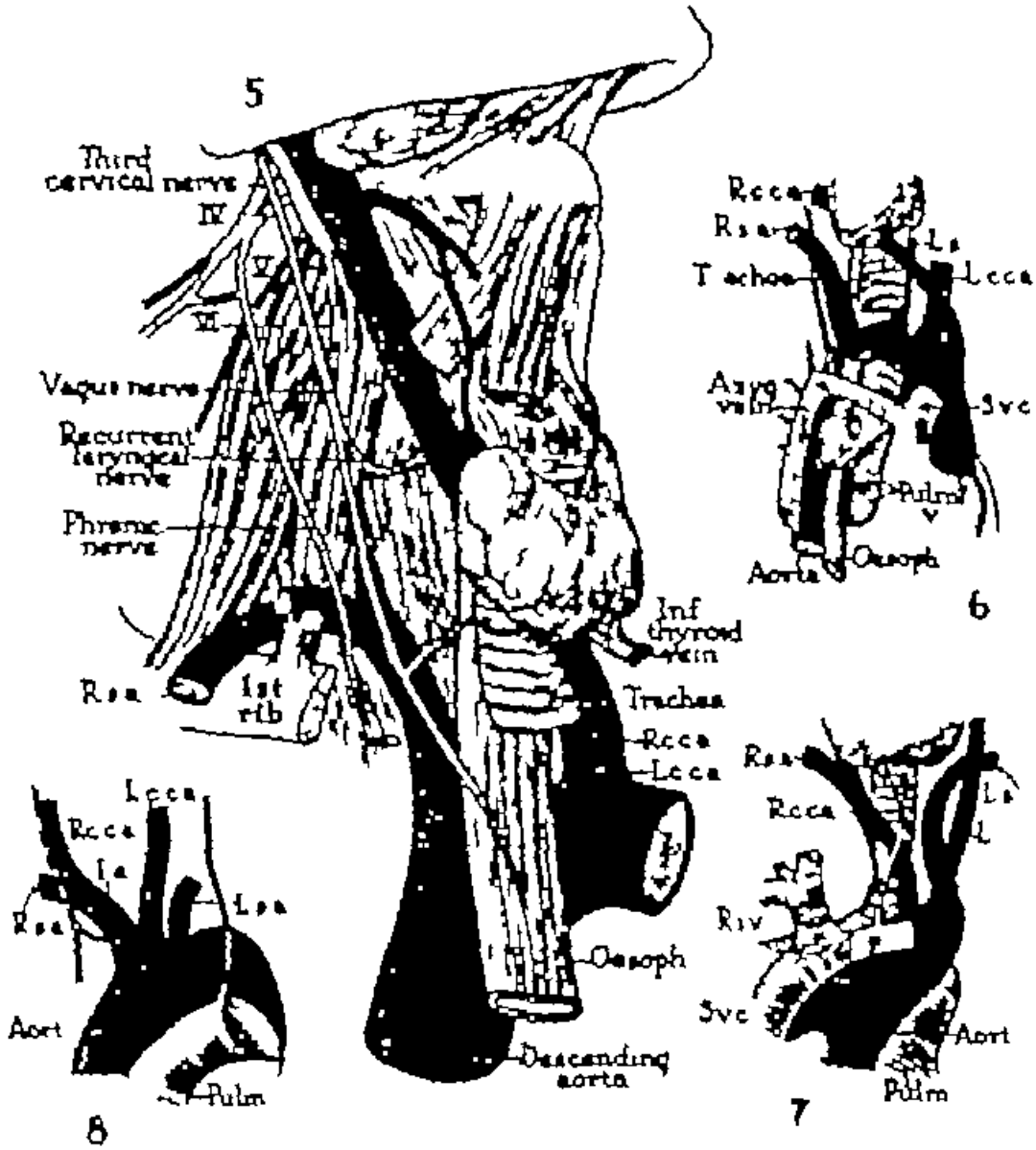

Fig. 5. The structures illustrated in Figure 1 as seen in ventrolateral view. Showing particularly the relation of the right common carotid to the thyroid gland and trachea, and of the anomalous right subclavian artery to the esophagus. × 44.

Fig. 6. The deep structures of the neck and upper portion of the thoracic mediastinum in lateral view (specimen III). Sections of the trachea and esophagus have been removed to reveal the situation and course of the anomalous right subclavian artery; the right recurrent laryngeal nerve is not looped around the latter vessel. ×

Fig. 7. The same structures in ventral view. Showing the relations of the carotid and subclavian arteries. The left anomalous vein has been cut just beyond the point at which it receives the inferior thyroid vein; a section of the trachea has been removed to show the esophagus as it lies in front of the right subclavian artery. × 22.

Fig. 8. The order and relations of the arterial trunks from the aorta, in a normal case. Contrast with Figure 2 showing anomalous arrangement, and compare with Figure 5, representing mechanism of origin. × 1.

aortic arch is lost in this transformation; the inferior laryngeal nerve of the right side passes directly to its termination, without passing around the right subclavian artery (compare Figs. 6 and 8).

As a result the anomalous vessel is situated *dorsal to the esophagus* (esp. Figs. 1, 2, and 5); instead of ventral to the trachea, the first vessel from the arch—the right common carotid artery—is drawn into a location beneath the corresponding lobe of the thyroid gland (Figs. 1 and 5); the recurrent laryngeal nerve of the right side follows a direct

high course from the vagus nerve to the larynx (Figs 1 and 5) The right subclavian artery is, then, not encountered on an anatomical level just dorsal to that of the innominate veins, but in retro-esophageal position against the vertebral column, the course of the right common carotid artery is not wholly to the right of the midline of the neck, but transtracheal, in a direction upward and toward the right, the recurrent laryngeal nerve does not descend to a clavicular level at the root of the neck, but only as far as the midthyroid level

Various clinical symptoms may arise from the relation of the anomalous vessel to surrounding structures, visceral pressure upon the right subclavian artery may produce inequality in radial pulses according to Harvey (1917) and others, through the same mechanism enlargement of the thoracic duct may occur, Cobey (1914) points out that, owing to pressure exerted upon the artery by the esophagus, its symptomatology may be confusingly similar to that of cervical rib, he infers that trophic changes in the upper extremity might follow Quain, long ago, mentioned dysphagia as one of its symptoms, citing a case history In surgery of the cervical region it may prove of importance in ligation of the subclavian artery because of the depth at which the vessel is situated (Goldbloom) In surgery of the upper esophagus (Harvey), and, in fact, in any approach to the right side of the neck, the peculiar position of the inferior laryngeal nerve would prove baffling Certainly in 2 of our cases (Figs 1 and 6) the relations of the common carotid artery to the right lobe of the thyroid gland would have been an anatomical condition fraught with surgical danger had a thyroidectomy or a low tracheotomy been performed

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TUMORS OF THE SPERMATIC CORD EPIDIDYMIS AND TESTICULAR TUNICS

Review of Literature and Report of Forty-One Additional Cases

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TUMORS of the testis are relatively rare They constitute 5.8 per thousand of all malignant tumors of men, according to the mortality statistics of the United States registration area Similarly tumors of the epididymis are exceptionally rare in fact so rare that their existence might seem of more academic than clinical importance Other intrascrotal tumors of interest, which occur more frequently include those of the spermatic cord and the testicular tunics.

The majority of tumors of the epididymis, spermatic cord and testicular tunics are of the benign type and hence the prognosis is quite different from that of testicular tumors. It seems worth while therefore, to call attention to this group of cases. This paper reviews the literature and presents 41 such cases seen at the Mayo Clinic before January 1 1935. Among the 41 cases there were 26 tumors of the spermatic cord 13 of the epididymis and 2 of the tunica vaginalis.

Hinman and Gibson in 1924, reviewed the literature up to that time and added 3 cases which they had observed. These are included in the following review

TUMORS OF THE SPERMATIC CORD

According to Patel and Chalier the earliest known tumor of the spermatic cord was recorded by Cloquet in 1819 This was a lipoma and may not have been truly a tumor of the cord for the report is meager Patel and Chalier collected 110 cases of tumor of the spermatic cord in a very complete review of the literature Among these were the following lipomas, 37 sarcomas, 22 mixed tumors, 33 fibromas 12, myomas, 5 and carcinoma, 1

Rubaschow (35) in 1926 reviewed the literature again and listed the following tumors of the spermatic cord reported up to that time teratoma, 1 dermoids, 13 mesodermal tumors, that is myxolipomas myxofibromas, myxofibrolipomas, myxofibrosarcomas, and so forth 27 cysts of the wolffian body 15 carcinomas, 3 lipomas, 57 fibromas, 24 myxoma, 1 sarcomas, 24 connective tissue cysts, 8 lymphangiomas, 4 and tumors of undecided origin (description inadequate) 6 or a total of 183

MacKenzie in 1932 in reporting a case of fibromyxosarcoma, discussed 14 additional cases which he had found in a review of the literature. MacKenzie included a case described by Oehlecker as a tumor of the spermatic cord which I believe should be classified as a tumor of the tunica vaginalis and it is so classified in this review He failed to include cases reported by Fritzler 3 cases of lipoma and 1 of sarcoma by Starlinger in 1925 a case of myxofibroma by Romiti, in 1927 3 cases, 1 of fibrosarcoma 1 of myxolipoma, and 1 of malignant tumor of connective tissue origin Salnelikikowa, in 1929, a rhabdomyosarcoma of a youth 15 years of age by Allende and Gonzalez, in 1930 a sarcoma by R Scotte Douglas, in 1930 a spindle cell sarcoma. Since the appearance of MacKenzie's article, cases have been described by Monserrat and Galvez, in 1932 a case of fibroblastic sarcoma of the cord by Cilento in 1932 an angioma by Deutsch, in 1933 a fibroma by Gioia, in 1933 a case of fibroma Gioia also mentioned in his article a case reported by Odena in which the tumor a lipofibrosarcoma, weighed 8 5 kilograms. In 1934 Hirsch reported a rhabdomyosarcoma, Leriche a reticulosarcoma and Fresnais and Mouchet a sarcoma These cases, added to those of MacKenzie's review would bring the total number of tumors of the spermatic cord which have been so far reported to 216

It is probably not commonly appreciated that these tumors sometimes attain enormous

size The largest growths, composed purely of lipomatous tissue or of a mixture of tissues, so called myxolipomas or myxofibrolipomas, may become quite annoying because of their size The case of Mazzini is one of the largest, the tumor, which completely obscured the genitalia, was larger than the patient's head Dermoids of the spermatic cord also attain fairly large proportions

Growth of the majority of tumors of the spermatic cord is extremely slow As a rule they are not painful, and frequently the patient is not aware of their existence until the trauma calls attention to them Following this they are, in most instances, allowed to attain an appreciable size before medical advice is sought, at which time the weight of the tumor causes local discomfort and perhaps a drawing pain in the groin

Benign tumors Approximately 70 per cent of these tumors of the spermatic cord are benign, as can be seen in the lists that have been given earlier in this paper Of the benign tumors, the lipomas, mixed mesodermal tumors, and fibromas make up the bulk of the group

The malignant tumors are almost exclusively sarcomatous in type Only 3 cases of carcinoma have been reported Rubaschow (37) reviewed these cases and concluded that the growths probably originated from cell-rests of the wolffian body No cases have been reported of neoplastic proliferation of the epithelium of the ductus deferens

It appears, then, that the majority of these tumors of the spermatic cord are benign, according to the reports in the literature, and this coincides with the experience at the Mayo Clinic, where, up to January 1, 1935, 24 patients suffering with benign tumors and 2, with malignant growths, were observed In 21 cases, the enlargement proved to be a lipoma of the spermatic cord The tumors varied from 2 to 8 centimeters in diameter The youngest patient was 33 and the oldest 67 years of age

Lipoma is the most commonly found tumor of the spermatic cord However, it does not occur with the frequency that might be expected when the fatty growths that have been encountered in the inguinal region are recalled to mind Such growths spring from the subserous fat around the margin of the internal inguinal ring, and in enlarging they grow along the inguinal canal, distending it, often the growths follow the spermatic cord as far as the scrotum In many cases these growths act as predisposing causes of hernia, not only because they distend the inguinal canal and the internal and external rings, but they will by propulsion, produce an infundibulum in the peritoneum and thus a hernial sac

When the growth is small, it is easy to distinguish at operation between the true lipoma of the spermatic cord and the more common lipoma of the properitoneal fat If, however, the tumor is large, it is often impossible to say that its origin is not from the spermatic cord A lipoma of the spermatic cord always should be surrounded by the tunica vaginalis communis and should derive its main blood supply from the vessels of the cord, but in time the true lipoma of the cord often will break through the tunica vaginalis communis and will connect so closely with the properitoneal fat that it appears to be of that origin

In this series of 21 cases of lipoma of the spermatic cord, there were 14 cases in which there was associated inguinal hernia In 5 cases there were apparently bilateral tumors, all in association with hernia It is my impression, from study of the records of these cases, that all of the growths were true lipomas of the spermatic cord Since more than 7,000 operations for inguinal hernia have been performed at the Mayo Clinic in the period covered by this review of tumors of the spermatic cord, it can be seen that the incidence in this experience is not high In every instance the surgeon gave the opinion that the lipomas originated from the spermatic cord

Microscopically the tumors were composed of fat tissue no different from that seen elsewhere in the body

Considering these 21 cases as instances of true lipoma of the spermatic cord, the approximate incidence of lipomas compared to all tumors of the spermatic cord recorded in the literature, and included in this paper, is about one to three, since there were 82 lipomas out of a total of 242 tumors of the spermatic cord (33 8 per cent)

Fibroma of the spermatic cord occurs about a third as frequently as lipoma. Rubaschow (37) listed 24 cases which he collected from the literature and since that time only 5 other cases have been reported namely by Gloia and by Deutsch

Fibromas of the spermatic cord are usually small but cases have been reported in which the size attained was unusual, and in 1 case the tumor weighed 15 kilograms.

According to Patel and Chalier and Rubaschow (37) the origin of these fibromas appears to be in that portion of the spermatic cord that is near its *juncture with the epididymis*, and they arise from the connective tissue which unites the various elements of the cord at that point. They are slow growing and cause no symptoms other than the swelling This is indicated by the fact that the majority of the patients give histories of having noted the tumors for a number of years before seeking medical attention the average interval is 6 years.

CASE 22[1] A man, 28 years of age, as long as he could remember had noted a mass in the right inguinal region near the external inguinal ring He was certain that it had not increased in size for many years He was advised to have it removed At operation the growth was found to be attached to some of the spermatic veins It was lobulated, measured approximately 4 by 3 by 2 centimeters, and weighed when excised, just 14 grams On gross appearance it was firm and on inspection of its cut surface, seemed fibrotic Microscopic examination proved it to be a fibroma Convalescence was uneventful and the patient was alive and well when heard from 4 years later

True myxoma of the spermatic cord is an extremely rare type of tumor The case of Schulter is the only one in which the growth can be correctly termed a myxoma Rubaschow (37) reported 27 cases which he classified as *tumors of mesodermal origin* These were reported by the various authors as myxolipomas, myxofibromas myxofibrolipomas, myxosarcomas, myxochondrosarcomas myxocystosarcomas, osteomas, osteosarcomas and fibroliposarcomas To these should be added similar cases reported by Starlinger Romiti and MacKenzie That many of these tumors are relatively benign is suggested by the case included in MacKenzie's review reported by Mannini in which the growth, a lipofibromyxoma, attained huge size without apparent toxic effect. It is safe to say that not more than half of these combined tumors are very malignant in character

Patel and Chalier collected from the literature reports of 5 cases of myoma of the spermatic cord One of the patients seen at the Mayo Clinic could be considered to have had a myoma. However because the growth recurred and because there were in some portions rather numerous mitotic figures, it was classed as a *myosarcoma of low grade of* malignancy Myomas arise in the region of the juncture of the ductus deferens and the epididymis, and in most cases are adherent to both. Muscle fibers of the cremasteric internus muscle are the apparent origin. They do not attain the huge size of the lipomas and are more firm on palpation but not as hard as fibromas.

Vascular tumors such as lymphangiomas, arising in the spermatic cord are rare. MacKenzie listed 5 cases and to these should be added a case reported by Cilento

CASE 23 A boy 5 years of age was brought to the *Mayo Clinic with a complaint of ear trouble.* This was cared for but routine physical examination disclosed a small mass in the left side of the scrotum, well above the testis Excision was advised, and at operation the mass, 1 centimeter in diameter was found attached to the spermatic cord just below the external inguinal ring On microscopic section it proved to be a hemangioma Convalescence and the subsequent course were uneventful

Only 13 cases of dermoid cyst of the spermatic cord are included in Rubaschow's report No other cases have been recorded since then. The spermatic cord is an unusual situation for a dermoid cyst. Theoretically these cysts arise from the primitive ectodermal cells displaced in the embryo from the lumbar region through the wolffian body These cells accompany that organ as rests, in its ultimate transition to the ductus deferens. In none of the cases reported was a diagnosis of dermoid made before operation

Benign cystic tumors of other nature include those arising in cell rests of the wolffian body and those in which the origin is uncertain, apparently arising from connective tissue

[1] Case 22 Fibroma of the cord

adjacent to the spermatic cord One such case was encountered at the Mayo Clinic and is described as follows

CASE 24 A man, 56 years of age, came for general examination This revealed, among other abnormalities, a small lump in the right side of the scrotum, apparently attached to the spermatic cord well above the upper pole of the testis After his attention was called to it, he admitted having known of its presence for years, but he had attributed no significance to it In the absence of symptoms he refused operation Two years later he returned, stating that he thought the growth had undergone recent enlargement, but examination did not confirm his impression, in the opinion of the examining physician However, he asked to have it removed Operation was performed through a scrotal incision, and an encapsulated growth, 2 centimeters in diameter, was found attached to the cord, well above the globus major of the epididymis On microscopic section the growth proved to be a cystadenoma and apparently originated in connective tissue

Malignant tumors The most frequently occurring malignant tumor of the spermatic cord is the sarcoma Twenty-four cases were reported up to 1926, and since then cases have been reported by Fritzler, Romiti, Karo, Allende and Gonzalez, Douglas, Leriche, and Fresnais and Mouchet Beyond any doubt, under the heading of malignant tumors, should be included also many of those tumors which are in part sarcomatous, such as myxosarcomas, liposarcomas, chondrosarcomas, fibrosarcomas, rhabdomyosarcomas, and various other combined growths The malignant nature of these tumors is sometimes overlooked It is impossible to estimate the grade of malignancy from a study of photomicrographs that accompany the articles Careful cytological study no doubt would disclose that some of them were relatively benign, however, the possibilities of transition in cell character as a result of stimulation by irradiation or injury always should be kept in mind and the growths treated accordingly Treatment ought to be similar to that employed for malignant tumors, with subsequent periodic observation In cases of highly malignant sarcoma, the clinical course parallels that of the most malignant tumors of the testis

Two cases of malignant tumor of the spermatic cord encountered at the Mayo Clinic follow

CASE 25 A man, 68 years of age, was first seen March 15, 1928, when he complained of bilateral inguinal hernias which he stated had been present for 12 years He had worn a truss for these hernias, and 4 months previously he had noted a hard lump forming at the right external inguinal ring, which was tender when the truss was in place, therefore he had discontinued use of the truss Examination disclosed a mass the size of a large plum (about 5 centimeters in diameter) at the right external inguinal ring It was firm and did not transmit light Roentgenograms of the thorax and spinal column were negative In addition to the tumor there were bilateral inguinal hernias Physical examination otherwise gave essentially negative results A diagnosis of bilateral inguinal hernia and of tumor of the right spermatic cord was made, and operation was advised Right herniotomy and right orchidectomy were performed April 10, 1928 A large tumor was found just at the external ring and extending over the symphysis pubis, arising from the cord 4 inches (10 cm.) above the testis Castration was performed and a portion of the cord was removed The hernial sac was excised and the canal completely closed by suturing the internal and external oblique muscles down to Poupart's ligament. The tumor removed is represented in Figure 1a Examination disclosed that the growth was very firm On cut section, in the gross, it had a yellowish-white, striated appearance such as is seen in uterine fibroids The testis, epididymis, and ductus deferens were not involved The tumor was very intimately attached to the spermatic cord

Microscopic section disclosed what seemed to be a typical fibroma, on close examination of the section, however, it was seen that the tumor, in some places, was cellular, and here and there a rather large cell appeared, of a type that is never seen in a typical fibroma such as, for instance, a uterine fibroid Because of this appearance the diagnosis of fibrosarcoma of malignancy grade 1 was made (Fig 1b)

The patient had an uneventful convalescence and returned home after 3 weeks, feeling well

The patient returned to the clinic 1 year later, or in May, 1929, complaining that 3 months after operation he had noted a recurring mass in the right inguinal region This had grown to approximately 10 centimeters in diameter in the 9 months following, a size much greater than the original tumor A diagnosis of recurrent malignant tumor was made and treatment by roentgen-rays and radium was given The mass continued to enlarge, and 2 months later attained such a size that it extended across the entire right lower quadrant of the abdomen The decision was made that the only justifiable treatment was further irradiation, and this was given, but without result. The patient died at home on September 14, 1929

Postmortem examination was made elsewhere, but details of the findings were not obtainable A microscopic section of the recurrent tumor in the groin is shown in Figure 2 It can be seen that these

cells bear very little if any resemblance to those of the original tumor The tumor is a fibrosarcoma, *grade 3*.

It is interesting but hardly profitable to speculate as to what caused the transition from a tumor of malignancy grade 1 to a tumor of which the malignancy was grade 3 in the case just reported. Sarcomas of low grade of malignancy occasionally are observed to undergo change as a result of injury The probabilities are that there was local extension of a more malignant type of cell at the time of removal of the original tumor which however could not be seen at operation.

CASE 26. A man, 33 years of age, was first seen at the Mayo Clinic December 9, 1920, at which time he stated that he had been operated on in 1914, and again in 1917 for the removal of tumors from the left groin. These had been the size of a hen's egg (about 6 cm. long) and the size of an olive (about 3 cm long) respectively He was not told what the nature of the tumor was considered to be, but roentgen treatments were given after their removal Further swellings were not noted until 2 years later when a tumor the size of a pea (about 1 cm. in diameter) appeared in the left inguinal region and began slowly to increase in size. Two months before he came to the clinic he was given three treatments by roentgen rays and radium This did not affect the size of the growth It was not painful and caused no symptoms the swelling was the only abnormality

Examination revealed an irregular hard, firm tumor measuring 6 by 2 5 centimeters, situated in the upper part of the scrotum and adjacent to the left external inguinal ring The testis and epididymis could be palpated separately and did not seem involved. All other physical examinations gave essentially negative results, including roentgenograms of the thorax and bones A diagnosis of tumor of the spermatic cord was made and operation was advised

Operation was performed December 20 1920, by Dr C H Mayo A mass the size of a lemon (about 7 cm long) was found involving the spermatic cord. The testis and cord were removed high in the inguinal canal

The tumor removed is represented in Figure 3a there were five separate lobulated masses, the smallest of which was 2 5 centimeters in diameter and the largest, 4 centimeters in diameter The tumor was pinkish white and very firm On cut section in the gross it looked fibrous On microscopic section the tumor was a typical myoma except that in places there were rather large cells, and mitotic figures could be found here and there Figure 3b represents an area such as makes up the greater portion of the tumor

The patient was given a treatment with radium because of the history of repeated recurrence and returned home feeling well. He was seen at the clinic again in August, 1923, or almost 3 years later he stated that a recurrence had been developing since December 1921 On examination, a mass of firm consistency measuring 10 by 4 centimeters was found occupying the left half of the scrotum and extending up into the inguinal region Examinations otherwise gave negative results, including roentgenograms of the thorax A diagnosis of recurring tumor of the groin was made.

August 24, 1923, the tumor was excised widely It involved the left groin and upper part of the scrotum, and when removed measured 7 by 4 by 4 centimeters, was very firm, and weighed 70 grams. On microscopic sections its structure was found to be very similar to that of the original growth, except that the cells were a little larger and the mitotic figures seemed of more frequent occurrence Figure 4 represents an area that is fairly typical of the entire tumor: the diagnosis was myosarcoma grade 1

The patient was given high voltage roentgen therapy and went home one month later In a letter received from him recently he stated that he is in good health and that the tumor has not recurred again.

TUMORS OF THE EPIDIDYMIS

Benign tumors Benign epithelial tumors of the epididymis are exceptionally rare. Sakaguchi in 1916 reported an adenoma of the epididymis of a man aged 32 years, who was operated on for long-standing thickening of that organ He referred to the tumor as an adenomyoma the principal tissue was glandular epithelium. This case is the only one of its type reported in the literature. Report of a case of benign tumor of the epididymis in which the predominating histological picture was that of epithelial hyperplasia follows.

CASE 27 A man 54 years of age entered the Mayo Clinic with a complaint of a nodule which had been present in the right side of the scrotum for approximately 25 years It had not caused symptoms until recently when he had noted pain in the right testis and groin Examination revealed a nodule approximately 2 centimeters in diameter in the upper pole of the epididymis Operation was advised The nodule proved to be attached to the epididymis and on the insistence of the patient unilateral castration was performed The testis proved normal. Microscopic section of the nodule revealed it to be a cystadenoma.

Lipoma is an exceptionally rare type of tumor Wilbolz has given the only report of a case up to the present time The epididymis normally does not contain fat, although occasionally a little may be found in the coverings

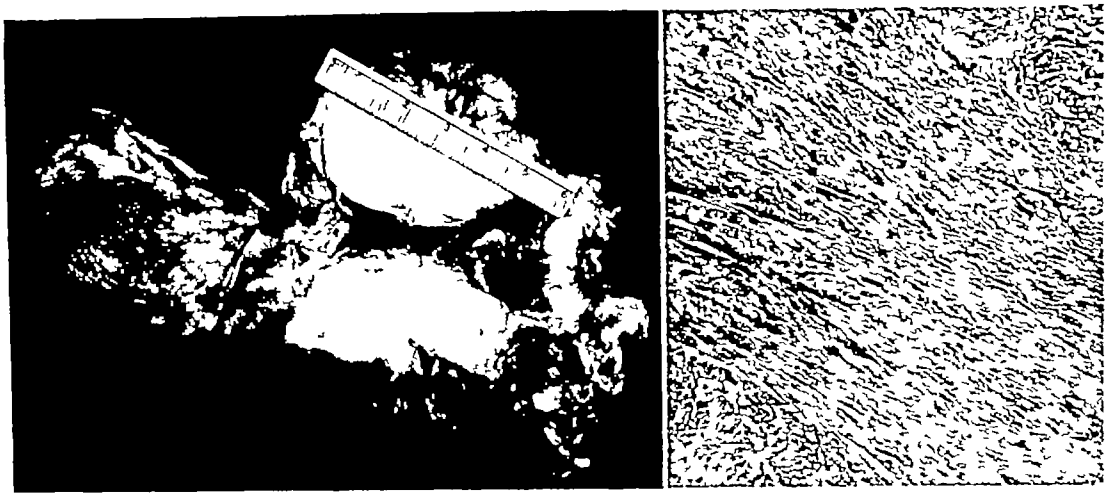

Fig 1 a, left, Fibrosarcoma of spermatic cord, b, section of same tumor, malignancy was graded 1 ×60

of connective tissue In Wilbolz's case the tumor apparently originated from fat in the connective tissue coverings as on section several small lobules of fat, varying in size from 5 to 7 millimeters in diameter, were found The pre-operative diagnosis in his case was epididymitis Lipoma of the epididymis is so rare that it is of no clinical importance

Myoma is the most common benign tumor of the epididymis if the site of origin can be proved satisfactorily to be in the epididymis Rubaschow (35), however, expressed the belief that these tumors arise from adjacent structures and not from the epididymis This is mere speculation, unless one has the opportunity of examining the tissue Hinman and Gibson listed 6 cases of leiomyoma which they collected from the literature and which seem acceptable To these should be added those of Eisenstaedt and Fischer, as these tumors certainly seem to have originated in the epididymis

The epididymis has been said to have been the site of origin of fibromas in several cases reported The tumors, however, originated in the caudal portion of the spermatic cord rather than in the epididymis and hence should be classed as tumors of the spermatic cord Hinman and Gibson and Rubaschow concluded, after careful study, that there is no report in the literature of an unquestionable case of fibroma of the epididymis There has been none since their articles appeared

Of the vascular tumors of the epididymis, Conforti, in 1910, reported a case of lymphoendothelioma, Hardouin, in 1911, a case of angioma, Rigano-Irrera, in 1925, a case of lymphangioma, and Marcandier and Thomas in 1930, a lymphangioma All these seem to be authentic, the tumors arising in the epi-

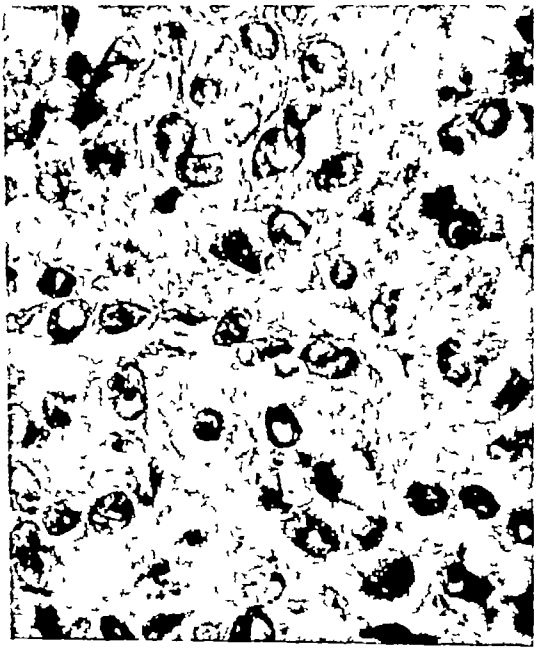

Fig 2 Fibrosarcoma, grade 3 ×500

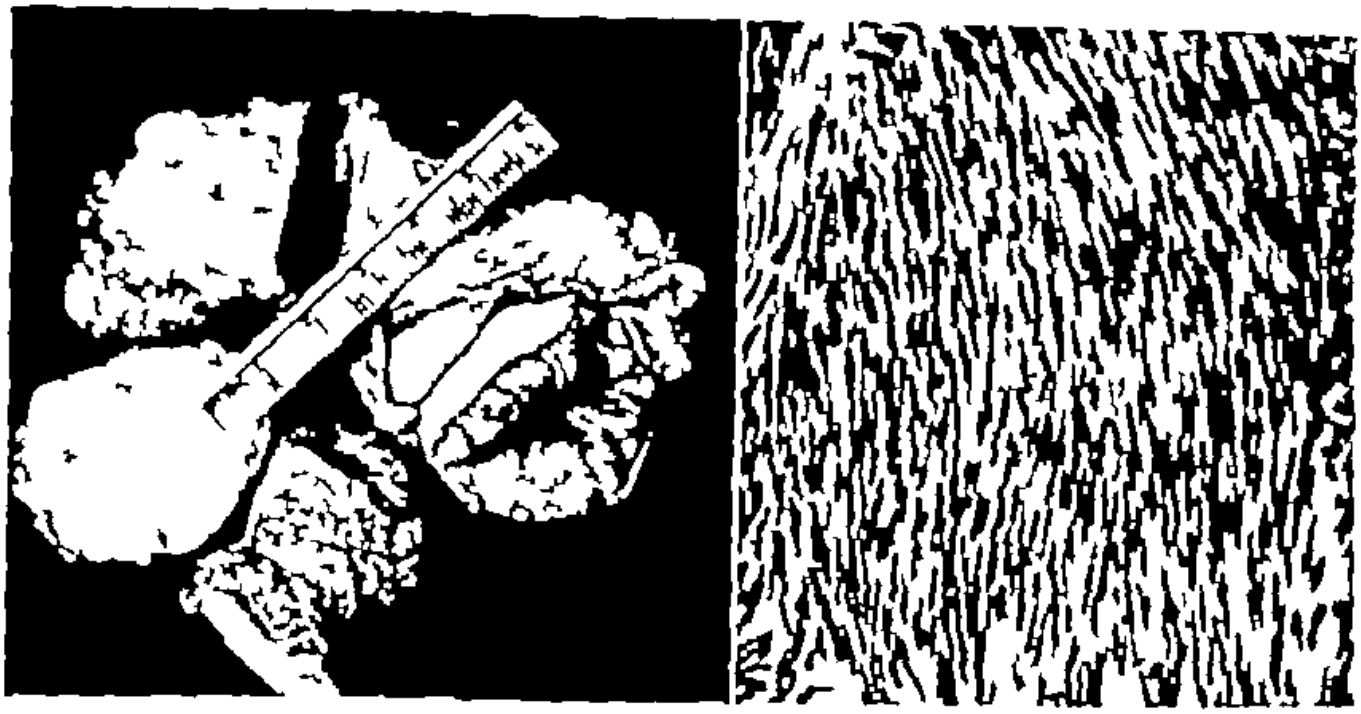

Fig 3 a, left, Myosarcoma of the spermatic cord b, section of same tumor malignancy was graded 1. X350

didymis. Four cases have been seen at the Mayo Clinic as follows

CASE 28. A man, aged 42 years, came to the clinic June 16 1919, *complaining of a lump on the left*

Fig 4 Myosarcoma, grade X900

testis which he first had noticed 4 years previously and which had increased slowly in size. Two years before he came for examination he had had a slight pain, lasting a few days, and the week before admission pain had been noted again On arrival here, however it had subsided again Examination revealed enlargement of the left epididymis to approximately 1 2 centimeters Physical examination otherwise gave essentially negative results A diagnosis of chronic epididymitis was made and operation advised.

Left epididymectomy was performed, as the left epididymis was replaced by a tumor Then a bottle operation was done to prevent development of hydrocele On gross examination, the tumor was found to measure 3 by 2 centimeters, and when sectioned it was grayish-white the periphery of the tumor was darker than a portion in the center which was 1 5 centimeters in diameter Microscopic examination revealed the tumor to be an angioma with marked hyperplasia of the endothelium This central hyperplasia was the cause of the difference in color observed grossly The low power photomicrograph (Fig 5a) was taken at a point which includes part of the darker edge and also a portion where there was endothelial hyperplasia The individual endothelial cells can be seen in a section of the center of the tumor (Fig 5b) A diagnosis of angioma with endothelial hyperplasia was made. The patient was entirely well when heard from 5 years after operation

CASE 29 A man, aged 31 years came to the clinic February 5, 1922, *complaining of a lump in the* right testis which he first had noted 6 years previously This gradually had increased in size until on admission it was approximately 2 5 centimeters

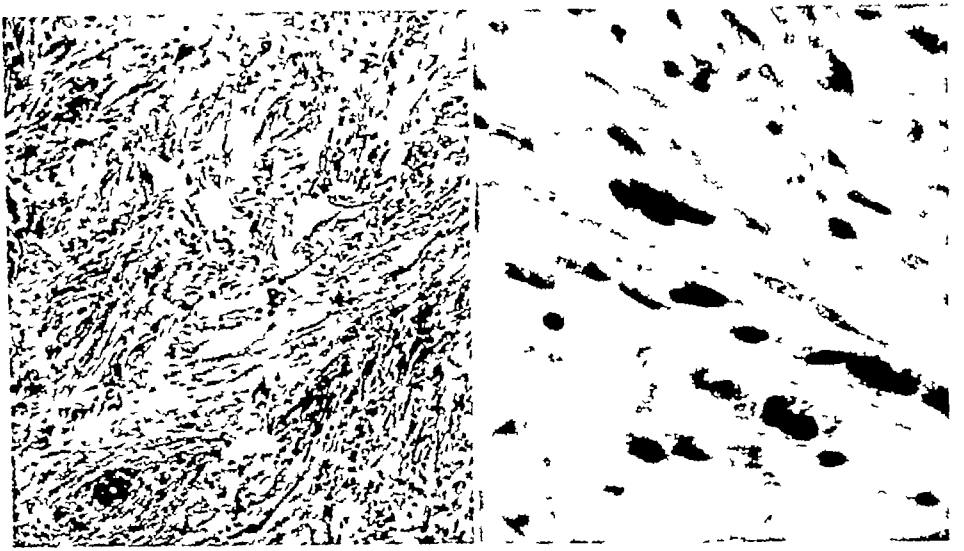

Fig 5 a, left, Edge of tumor and endothelial hyperplasia. ×85, b, central area of same tumor, with endothelial cells. ×425

in diameter It had never been painful and there were no other complaints Examination revealed an enlargement approximately 1 inch (2 5 cm) in diameter, of firm consistence, attached to the globus major of the epididymis Results of all other examinations were essentially negative A diagnosis of spermatocele was made and operation was advised

At operation a small nodule was excised from the lower pole of the right epididymis through a right, semilunar incision and Andrew's "bottle" operation was performed The tumor measured 2 by 1 5 centimeters and on gross and microscopic examination proved to be a lymphangioma Convalescence was entirely uneventful and the patient is well

CASE 30 A man, aged 25 years, was first seen December 23, 1921, when he complained of epigastric distress, such as is experienced by patients who have peptic ulcer He also complained of enlargement of the left testis which had developed after trauma 11 years ago

On examination, the left testis was about twice normal size Transmission of light could be demonstrated, and there seemed to be a hard mass fixed to the testis in the normal position of the epididymis Roentgenologic examination of the stomach disclosed a duodenal ulcer Operation for both lesions was advised

Gastro-enterostomy was performed for the duodenal ulcer and an angioma ¾ inch (1 9 cm) in diameter was removed from the epididymis and an Andrew's "bottle" operation for hydrocele was done Grossly the tumor measured 2 by 1 5 centimeters and was lobulated Microscopic section showed the tumor to be composed of hundreds of blood vessels, most of which were filled with blood All sizes of vessels were found and the intervening stroma consisted of the same types of cells that made up the vessel walls A diagnosis of hemangioma was made (Fig 6)

Convalescence was uneventful and the patient was in good health in 1928 when last heard from

CASE 31 A man, aged 44 years, had noted a swelling in the right testis for 5 to 6 years This had been without symptoms until shortly before examination, when it had seemed to enlarge slightly and the swelling had become slightly painful Examination revealed a small, nodular swelling in the lower pole of the right epididymis At operation, this was found to be intimately related to the epididymis and firmly fastened to the adjacent tunica albuginea It was 12 millimeters in diameter Microscopic section proved the growth to be a hemangioma

These vascular tumors of the epididymis are small None of the tumors in the cases reported in the literature attained the size of other tumors of the epididymis They are slow-growing, cause few symptoms, and apparently do not recur

Hinman and Gibson stated that they were unable to find a case of dermoid cyst of the epididymis reported in the literature Rubaschow did not mention a case, and after careful search I have concluded that there is no case of this sort on record A patient has been operated on at the Mayo Clinic for dermoid cyst of the epididymis The detailed report of the case follows.

Fig. 6. Hemangioma of epididymis.

Fig. 7. Dermoid cyst of epididymis.

CASE 32. A man, aged 25 years, came to the clinic February 2, 1921, complaining of a swelling in the right groin which had been developing for the past 10 years. Four years previously, there had been a discharge of thick material from the scrotum and this had continued up to the time of admission. Occasionally there had been slight discomfort, but never any acute pain. There had not been any urinary symptoms.

Examination disclosed an enlargement of the right testis to three times normal size with multiple sinuses in the scrotum from which a foul discharge exuded. The right ductus deferens felt nodular, and the enlargement seemed to be principally of the epididymis. Urinalysis was negative as were all other examinations. A diagnosis of tuberculous epididymitis, with multiple sinuses, was made and operation advised.

Right epididymectomy and vasectomy were performed. The growth proved to be a dermoid cyst containing hair, a tooth and very foul, thick pus. The sinuses in the scrotum were adherent. The testis was somewhat atrophic and was not removed. The entire epididymis and a portion of the ductus deferens were excised. Gross examination of the tissue revealed it to be made up of epididymis which was cystic in portions. There were several sebaceous cysts, encapsulated by epididymal tissue. The white portion at the top of Figure 7 is a sebaceous cyst. The duct of deferens can be seen just below this, and in the lower half of the figure a lock of hair. A fully developed tooth can be seen just to the right of the hair.

The patient's convalescence was entirely uneventful. He reported, 3 years later, that he was in excellent health.

According to the history, the patient first noted beginning enlargement of the epididymis at the age of 15 years. A roentgenogram might have shown the tooth and thus have been an aid in diagnosis, but as a dermoid cyst was not suspected, roentgenological examination was not made. This is an unusual case and apparently is the only one on record.

Calcified degenerated hematoma of the epididymis, or calcified hydrocele, easily can be mistaken for dermoid cyst. Three such cases have been seen at the Mayo Clinic. The absence of keratin makes the diagnosis of dermoid cyst impossible.

Martin and Sermet in 1932 reported 2 cases of cystic embryoma. These definitely seemed benign and should be classed as such.

Malignant tumors. Ferrier and Loonl in 1934 reviewed the literature and stated that including their own case, 15 cases of primary

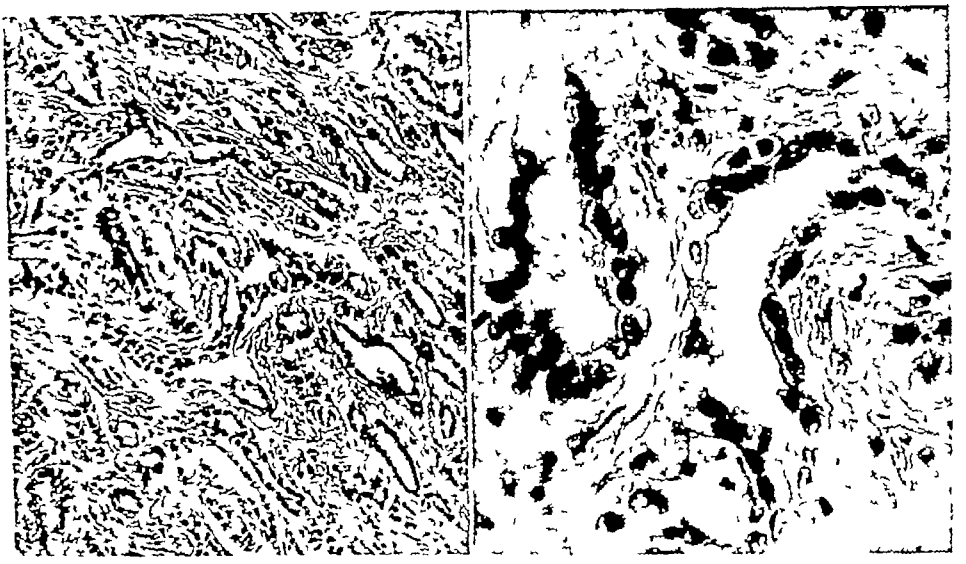

Fig 8 a, left, Adenocarcinoma, grade 1, of epididymis ×130, b, section of same tumor ×425

carcinoma of the epididymis had been reported De Vincentiis, about the same time, described a seminoma which can be similarly classed, bringing the total number of reported cases, to date, to 16

Seven cases of carcinoma of the epididymis have been seen at the Mayo Clinic Of these, 5 are of relatively low grade of malignancy and two are of high grade A description of each case follows

CASE 33 A man, aged 56 years, came to the clinic June 27, 1916, complaining of a swelling of the left testis, which he had noted for 6 years Recently the tumor had begun to increase in size to a noticeable degree There was also a slightly painful swelling in the right testis which had been present for 15 years

Examination disclosed a fluctuating, painless swelling around the left testis, which transmitted light, and a similar although smaller swelling around the right testis A diagnosis of bilateral hydrocele was made

Andrew's "bottle" operation was performed for bilateral hydrocele of moderate size and a small tumor of the lower pole of the right epididymis was found and excised On gross examination this tumor was bluish white in color and apparently was well encapsulated It was 7 millimeters in diameter Microscopic section of the tumor revealed a rather interesting structure Numerous acini lined with epithelial cells could be seen in the low power field (Fig 8a) Most of the cells were well differentiated but some of them had rather large nuclei which contained large nucleoli Since the tumor appeared to be fairly well differentiated it was diagnosed adenocarcinoma grade 1 It was a relatively benign tumor, but, nevertheless, an adenocarcinoma A photomicrograph of higher power is shown in Figure 8b

The patient had an uneventful convalescence and is well

CASE 34 A man, aged 27 years, came to the clinic September 3, 1918, stating that 7 years previously he first had noted slight enlargement of the right testis, and this slowly had increased in size One year previously a dull, intermittent pain in the testis had begun There were no other complaints On examination a firm swelling, about 2 5 centimeters in diameter, was found in the lower pole of the right epididymis Roentgenograms of the chest and bones, and the reports received on all other examinations were negative A diagnosis of tuberculous epididymitis was made

Partial epididymectomy was performed and a tumor about 1 inch (2 5 cm) in diameter was removed from the lower pole of the epididymis On gross examination the tumor, represented in Figure 9a, was firm, although not nearly as firm as a fibroma and was well encapsulated It had the appearance of malignant tissue Microscopic examination of the tissue disclosed it to be adenomatous in structure, and that rather loose, fibrous, interstitial tissue was present The glands were lined with definite epithelial cells, some of which were rather broad A close resemblance to mixed tumor was noted Figure 9b is a low power photomicrograph of a typical section of the tumor

The patient's convalescence was uneventful He returned home and on recent inquiry stated that there has been no recurrence and that he is in good health

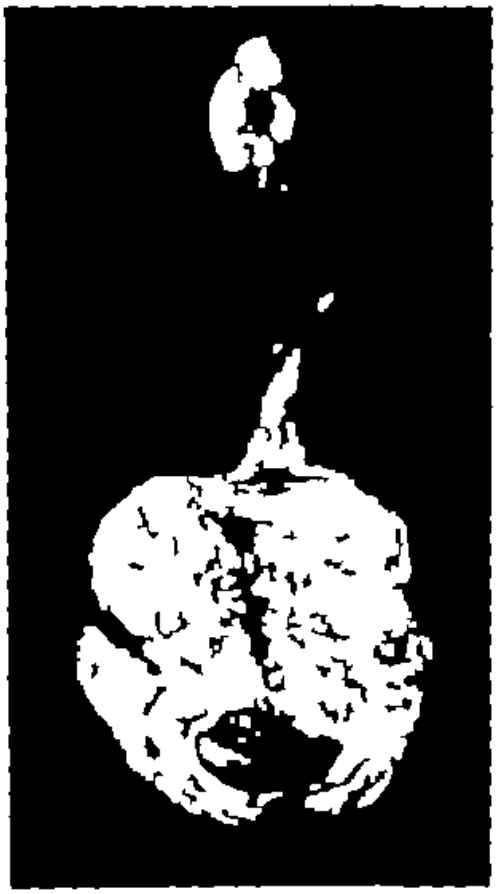

Fig 12 Carcinoma of epididymis

Comment From the review of the literature and from the foregoing cases tumors of the epididymis seem to occur in the proportion of 40 per cent benign to 60 per cent malignant. Of the 25 benign tumors 9 were adenomas, 1 was a lipoma, 8 were myomas, 8 angiomas 3 fibromas, 1 was a cystic dermoid and 2 were cystic embryomas. Of the 36 malignant tumors 23 were of epithelial origin 12 of sarcomatous type and 1 was a teratoma. The fact that about 40 per cent of these tumors of the epididymis are benign should be kept in mind in considering cases of tumor of the testis or what seem to be tumors of the testis The possibilities of a favorable prognosis following surgical exploration of what appears to be a testicular tumor should justify the urging of operation in all such cases unless metastasis to other parts of the body can be demonstrated

TUMORS OF THE TUNICA VAGINALIS

The tunica vaginalis is of far more importance than the tunica albuginea in regard to formation of tumor It is often very difficult, and sometimes practically impossible, to distinguish tumors of the tunica vaginalis from those arising in adjacent structures For this reason varying opinions as to the frequency of occurrence of these tumors have been expressed A tumor thought by an observer to arise from the tunica vaginalis may on review by another be classified as a tumor of the spermatic cord. From the review to follow It can be seen that the majority of the tumors are benign and that the total number reported in the literature is approximately 50

Benign tumors Only 3 authentic cases of lipoma have been reported in the literature. Park in 1886 removed a lipoma weighing 3 pounds (1.4 kg) from the right tunica vaginalis. The tumor was supplied with blood vessels from both the testis and spermatic cord and there were numerous fibrous trabeculae projecting from the testis out into the fatty mass. Placitell and Deming, in 1931 each reported a case of lipoma of the tunica vaginalis In the latter s case the lipomas were bilateral and quite small.

Hinman and Gibson stated that only 2 cases of adenoma have been reported in the literature, that by Muhsam, in 1898 and that by Nicolopoulo in 1895 A case which I believe should be classified as an adenoma follows

CASE 40 A man, aged 60 years, came to the clinic August 5, 1930 stating that he had suffered with a hydrocele for many years This had been aspirated on many occasions without incident, but 3 weeks prior to admission, a few days after aspiration had been performed, the scrotum had begun to swell rapidly and had become sensitive There were no signs of inflammation On examination, a rounded mass, about 7 5 centimeters in diameter was found in the right side of the scrotum with this exception the patient was in excellent physical condition Exploration was advised At operation, a thick walled hydrocele was opened readily, disclosing a cystic mass intimately attached to the parietal leaf of a thickened tunica vaginalis, just opposite the upper pole of the testis and the upper portion of the epididymis It was definitely encapsulated and was enucleated readily The thickened tunica vaginalis was cut away and the edges sutured to control oozing

The mass weighed 50 grams and measured 9 by 6 by 5 centimeters The cut surface of the tumor on gross inspection, presented an appearance somewhat similar t that of an adenoma of the thyroid gland

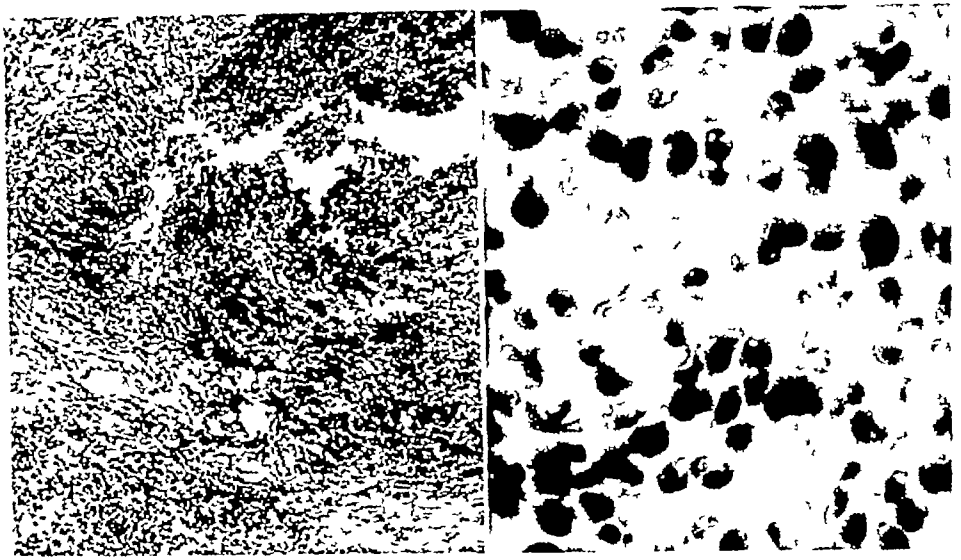

Fig 13 a, left, Carcinoma, grade 4 section of same tumor as that represented in Figure 12 ×65, b, section of same tumor ×600

It was more spongy in structure and the glandular portions contained a clear fluid, except in one part, in which the fluid was hemorrhagic This part might have been punctured by the needle when the hydrocele was aspirated The pathologist's report of the microscopic study of sections cut from the growth was hemorrhagic cystadenoma Convalescence was uneventful

Five cases of myoma have been reported in all of which the tumors probably had their origin in the gubernaculum

Of the vascular tumors Rindone, in 1901, reported a tumor originating in the tunica vaginalis which he regarded as lymphangioendothelioma Similar cases have been recorded by Micotti in 1926, and by Scarpello in 1927 Nora, in 1933, described an endothelioma

Rubaschow (36) in 1926 collected from the literature reports of 16 cases of fibroma which he was certain were tumors of the tunica vaginalis Since that time Stricker and Franck have reported a case in which the tumors were multiple Oehlecker in 1930 reported a case of a man, aged 26 years in which the tumor was found to be situated in the parietal leaf of the tunica vaginalis just above the upper pole of the testis, and to extend downward pressing on the testis While it might be considered as a tumor of the spermatic cord, it seems best to classify it as arising in the testicular tunic

A case of fibroma of the tunica vaginalis which came to operation at the clinic is described next

CASE 41 A man, aged 45 years, came to the clinic November 16, 1915, stating that he recently had noticed a small nodule in the right testis There had been no symptoms from this enlargement On examination, a nodule was found in the right epididymis or very closely adjacent to it It was firm, not tender, and approximately 1 5 centimeters in diameter All other examinations were essentially negative including roentgenograms of the chest A diagnosis of chronic epididymitis, which possibly might be tuberculous, was made and operation advised

Right epididymectomy performed, removing the ductus deferens up to internal ring As a small hydrocele was present, corrective operation was done

The tumor, on gross examination, had the appearance of a fibroid and was well encapsulated It arose intimately from the dense inelastic fibrous tissue surrounding the epididymis and was attached to it. The tumor did not encroach on the tubules making up the epididymis and could be pulled away from the body of that organ The fibrous tissue investing the epididymis was very tough and inelastic and was apparently the visceral layer of the tunica vaginalis, normally found there From this the tumor was sharply demarcated and yet was densely adherent to it A capsule separated the tumor from the epididymis (Fig 14a) Microscopic section revealed the growth to be a typical fibroma (Fig 14b) The patient made an uneventful convalescence.

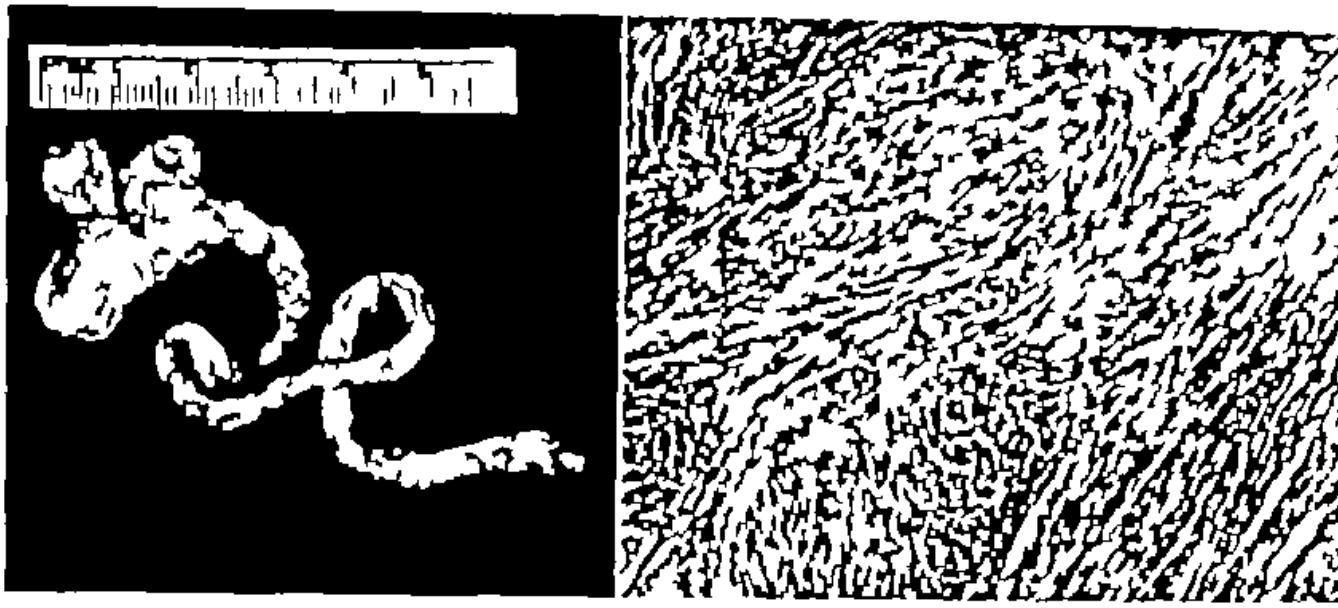

Fig 4 a, left, Fibroma of the tunica vaginalis, b, section of the same tumor × 40

Malignant tumors Rubaschow (36) collected reports of 15 cases of sarcoma of the tunica vaginalis and to these the only cases to be added are those of Valdoni who reported a case of sarcoma of a patient 17 years of age, and of Donati who in 1934, reported a case of fibrosarcoma. Rubaschow (36) called attention to the fact that the majority of the tumors occur in very young individuals. Valdoni s patient was only 17 years old and in the 11 cases listed by Rubaschow (36) the oldest patient was only 35 years of age. Sarcoma of the testicular tunics is in this respect similar to that of the testis. On the other hand sarcoma of the spermatic cord rarely occurs in young individuals

TUMORS OF THE TUNICA ALBUGINEA

Only 4 cases of tumor of the tunica albuginea have been recorded in the literature They were included in the review of Hinman and Gibson In all of the cases the tumors proved to be fibromas The operation employed was castration In three of the cases, and in the other enucleation of the tumor which was small and well encapsulated, was possible.

CLINICAL DIFFERENTIATION OF TUMORS

Because of their rarity tumors of the structures considered in this paper are scarcely ever considered in the differential diagnosis of intrascrotal enlargements. In any given case tumor of the testis should be considered first If however the testis is found to be separate from the growth on palpation the interest lies in distinguishing the extratesticular scrotal tumors as a whole from the so called pseudotumors, such as hematocele and spermatocele One should also think of tuberculous epididymitis, traumatic orchitis with associated hydrocele or hematocele and acute hydrocele with torsion of the cord Lipomas of the cord are often confused with inguinal hernia. The fact that these tumors, often benign, simulate malignant tumors of the testis seems to be the chief point of interest.

TREATMENT

In all cases surgical exploration is the procedure of choice. Since a large percentage of tumors of the epididymis, spermatic cord, and testicular tunics are benign it is often possible to do a conservative operation Castration should not be performed until sections of the tissue have been studied under the microscope

If the tumor is found to be malignant local removal that is, castration followed by treatment with roentgen-rays or radium, seems to be all that is indicated The results of the so called radical operation, involving removal of retroperitoneal lymph tissue, do not justify its use.

SUMMARY AND CONCLUSIONS

Tumors of the epididymis, spermatic cord, and testicular tunics are extremely rare Twenty-six cases of tumor of the spermatic cord seen at the Mayo Clinic are reported, of these tumors 21 were lipomas, 1 was a fibroma, 1 a hemangioma 1 a cystadenoma, 1 a fibrosarcoma, and 1 a myosarcoma

Thirteen cases of tumor of the epididymis seen at the Mayo Clinic are reported Among these tumors there was one dermoid cyst, a hitherto unreported type of epididymal enlargement, 1 cystadenoma, 4 angiomas, and 7 carcinomas Of the 7 malignant tumors 4 were adenocarcinomas, grade 1 1 a carcinoma, grade 2, and 2 carcinomas, grade 4

Two cases of tumors arising in the tunica vaginalis are reported, 1 of the tumors was a fibroma and the other a cystadenoma

The following conclusions may be drawn

1 Approximately 70 per cent of all tumors of the spermatic cord are benign

2 Approximately 40 per cent of tumors of the epididymis are benign

3 Approximately 60 per cent of tumors of the testicular tunics are benign

4 The prognosis is more favorable in cases of tumor of the spermatic cord, epididymis and testicular tunics than in cases in which tumor originates in the testis, tumors of the testis are, almost without exception, highly malignant

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CLINICAL SURGERY

FROM THE MEMORIAL HOSPITAL

GASTROSTOMY IN THE MANAGEMENT OF GASTRIC AND ESOPHAGEAL CARCINOMA

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SEDILLOT, in 1849, was the first surgeon to attempt the formation of a permanent gastric fistula in the treatment of cancer of the esophagus and he gave to the procedure its present name—gastrostomy Twenty-six years later the first successful operation was performed, and since then many different types of gastrostomy have been proposed and described in the literature The usefulness of this operation has increased with the improvement in the type of procedure employed and with the general improvement in surgical technique

The ideal gastrostomy should provide a gastric fistula not affected by the action of gastric juices It must be continent and permit no leakage of gastric juices or ingesta It must also be permanent and so fashioned as to permit the patient easily to insert his own catheter for each feeding The stoma must be readily dilatable so as to allow repeated instrumentation through it, such as gastroscopy, retrograde esophagoscopy, and bougienage It is desirable that the operation lend itself well to local anesthesia. There should be no operative shock, and the procedure should be possible in the contracted stomach (due to disuse or disease located in the cardia)

The satisfactory gastrostomy must permit gastric digestion immediately and must not confine the patient to bed continuously more than 2 or 3 days after operation Of all the types so far devised the Janeway (1 and 3) gastrostomy most nearly fulfils the above requirements On the head and neck service at the Memorial Hospital this type of gastrostomy has become a common preliminary step in the treatment of carcinoma of the esophagus and cardia of stomach Since 1928 this operation has been carried out in 163 cases

OPERATIVE TECHNIQUE

Under local infiltration of the skin with 1 per cent novocain containing 10 drops of adrenalin to the ounce, together with intercostal nerve block of plain 1 per cent novocain, a longitudinal incision is made over the outer third of the upper left rectus muscle from the costal margin downward for not more than 6 centimeters The outer rectus fascia is incised and the rectus muscle split in the direction of its fibers The fibers of the transversalis muscle are incised in the direction of the incision and peritoneum infiltrated with 1 per cent novocain and opened

A brief and necessarily limited exploration of the anterior surface of the liver and the pre-aortic and perigastric regions for secondary deposits is carried out The anterior wall of the body of the stomach is usually found directly beneath the incision, but in thin patients with elongated, flattened chests and in patients with cancer of the cardiac portion the stomach may be situated rather high, but with slow gentle traction it has always been possible to deliver a sufficient portion of the anterior stomach wall into the wound Five Allis clamps are then applied outlining a rectangular flap 2 centimeters wide and 3 centimeters in length with its base directed toward the greater curvature, shown in Figure 1 The wound edges are carefully protected with small, thin, laparotomy pads, the outlined flap is quickly incised, and all bleeders are clamped and securely ligated The stomach may be found much contracted, particularly in its transverse dimensions, and, if so it will stretch markedly, this fact should be borne in mind when the flap is outlined

The closure of the defect is begun at the middle of the incision parallel with the lesser curvature, and is continued up along the edges of the flap to form a gooseneck tube A running suture of No 00 chromic catgut is used for this mucosal layer, and before it is entirely closed a No 12 French catheter is inserted into the stomach A running interlocked Lembert suture of No 00 chromic catgut is used to close the serosa The stomach

[1] From the Head and Neck Department of Memorial Hospital service of Dr Hayes E Martin

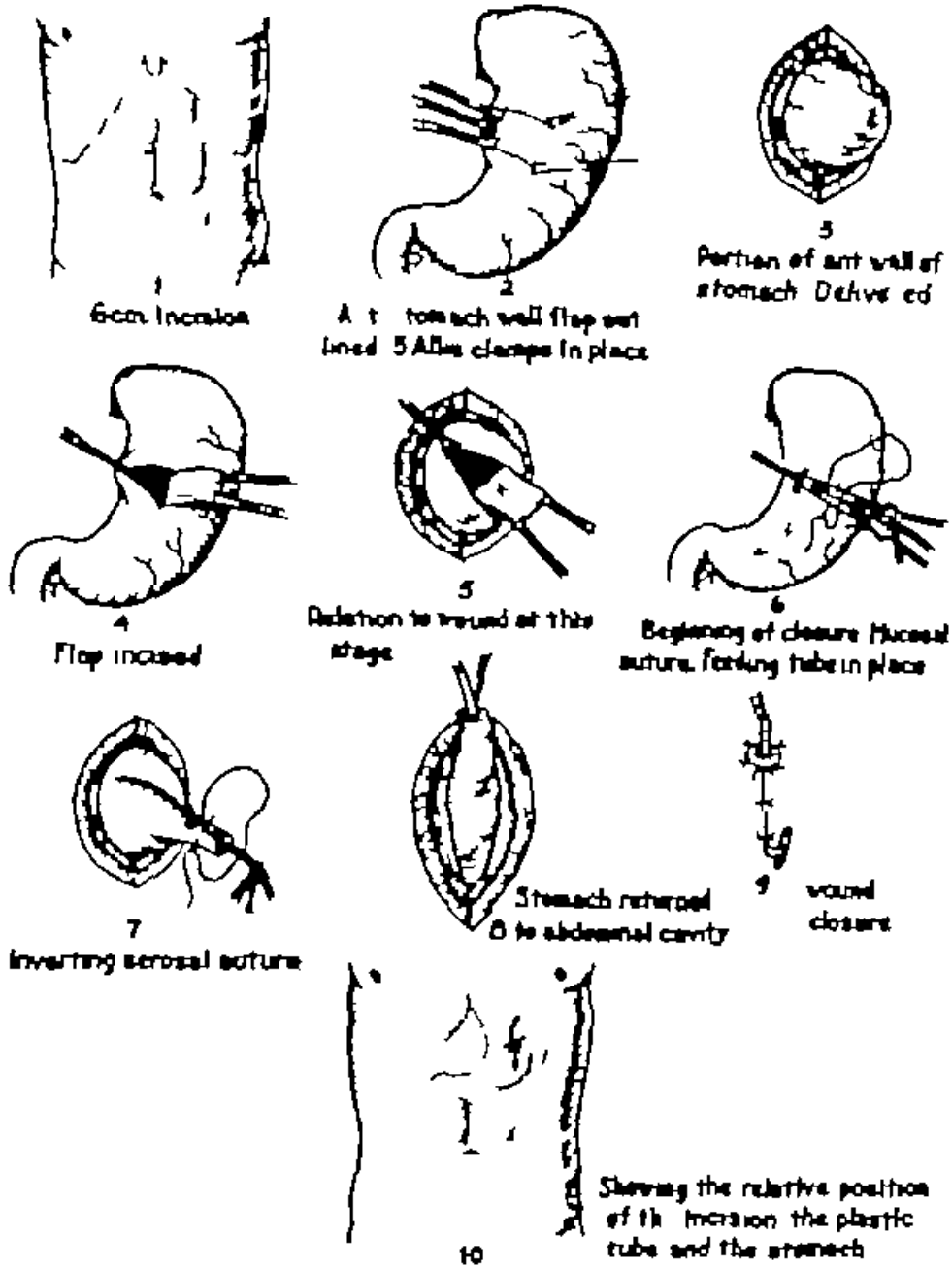

Fig 1 Jejunostomy Incision 2, Outlining of rectangular flap of anterior stomach wall—first incision parallel with lesser curvature 3, The anterior stomach wall has been drawn into the wound to prevent peritoneal contamination when the stomach is opened 4, Rectangular stomach wall flap incised 5, Relation of stomach to wound at this stage 6 Mucosa partly closed and No French catheter inserted 7 A running interlocked Lembert suture of No 00 chromic catgut closes the serosa 8, Gooseneck tube brought out through upper angle of wound 9, Mucosa sutured to skin edge and abdominal wound closed 10, Relationship of stoma to stomach and anterior abdominal wall

is then returned to the abdominal cavity the *operator and assistants change into fresh sterile* gloves and the wound is closed in layers An assistant holds the gooseneck tube with the suture line in contact with the upper wound angle. No. 1 plain catgut interrupted sutures are used for the peritoneum and transversalis muscle *One* loosely tied mattress suture of the same suture *material is used to approximate the cut edges of* the rectus muscle loosely over a small wick of iodoform gauze which is brought out through the lower angle of the wound The anterior rectus fascia is closed with interrupted No 1 chromic catgut sutures and *the posterior surface of the*

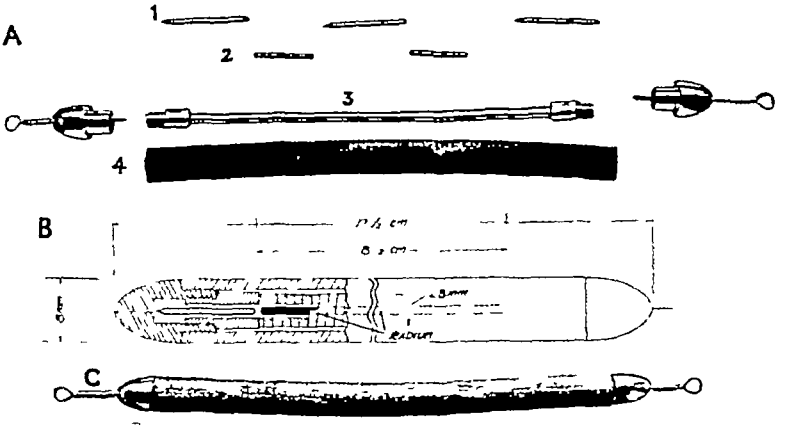

Fig 2 The esophageal radium element tandem A, Unassembled 1, Three radium element tubes of 10 milligrams each 2, Two dummy tubes 3, Flat wire stainless steel tubing with nickel steel end pieces 4, Black rubber tubing B, Mechanical drawing of tandem C, Tandem assembled ready for use.

gooseneck tube is anchored to this fascia by one suture of No 00 chromic catgut which passes through the serosal coat only The skin is closed with three interrupted, vertical, mattress sutures of medium dermal and the mucosa of the gooseneck stoma is fixed to the skin of the upper wound angle by four interrupted black silk sutures A dry dressing is applied and the feeding tube is fixed to the dressing in such a manner as to prevent it being accidentally withdrawn from the stomach

It is obvious that this operative procedure requires a little more surgical care and skill than is necessary in the simpler forms of gastrostomy, but this possible objection is outweighed by the more satisfactory postoperative results of the Janeway operation

The iodoform gauze drain is removed in 24 hours, the patient is out of bed on the second or third postoperative day, and the sutures are removed on the fifth postoperative day The postoperative care has been reported in the recent past (5) and will not be repeated here After 7 days the gooseneck tube is healed firmly and will permit gentle instrumentation through the stoma, and intra-esophageal radiation with the radium element tandem may be started without interfering in the least with the patient's nutrition

If gastrostomy is delayed until late in the course of the patient s disease then a definite, rather high, postoperative mortality must be expected, for a certain number of these patients are going to die of their disease within the period of postoperative convalescence Our previously reported (2) operative mortality of 5 8 per cent is the lowest recorded for gastrostomy and each fatality in our series was due to the patient s disease and not to the operative procedure

In order to maintain low morbidity and operative mortality rates, it has been learned from experience that certain factors must be observed The operation must be done under local anesthesia as general anesthesia in these elderly, dehydrated, and emaciated patients is hazardous and unnecessary The abdominal incision is limited to 6 centimeters because this will permit adequate exposure and at the same time minimize the danger of postoperative wound infection which, if it does occur, will be a small matter rather than one of serious import. Postoperative evisceration does not occur, and a small incision allows the patient to be out of bed safely on the second or third postoperative day The short incision will limit abdominal exploration, but this in turn will lessen postoperative reaction

From other clinics where the Janeway gastrostomy is being performed, there have come personal reports of sloughing of the terminal portion of the gooseneck tube There are three causes of this complication (1) The flap of anterior stomach wall is cut too long or too narrow or at right angles to its blood supply, which should come from the vessels of the greater curvature (2) The anterior fascia of the rectus muscle is sutured too snugly about the gooseneck tube and postoperative edema causes strangulation (3) The one suture used to anchor the tube to the anterior rectus fascia is placed too deeply and shuts off the arterial supply to the terminal portion of the plastic tube

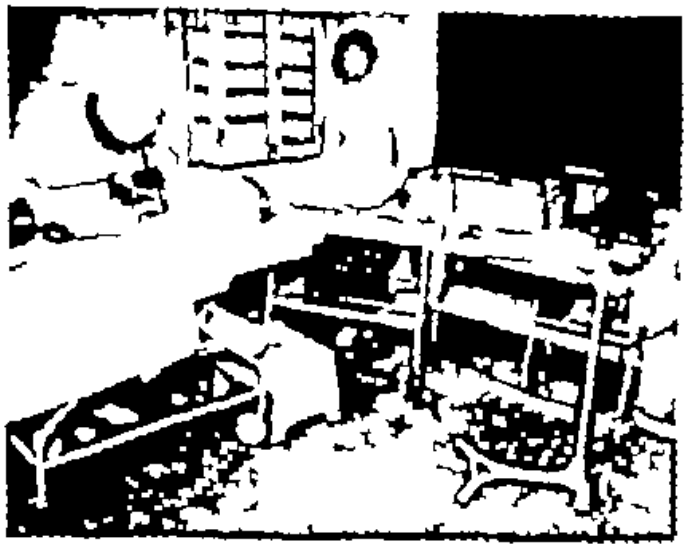

Fig. 3. An olive tipped bougie 4 has been introduced into the stomach and after the gastrostomy stoma has been dilated, a small esophagoscope is inserted into the stomach and the bougie is picked up

The stoma should be small and a small catheter (No. 12 French) should be used for feedings, as a larger tube will dilate the opening and permit leakage.

The value of gastrostomy in the treatment of gastric and esophageal cancer will depend largely on the care and skill with which the operation is carried out. A satisfactory gastrostomy is a very necessary preliminary step in the treatment measures to be described.

THE INTRA-ESOPHAGEAL RADIUM TANDEM

The tandem (Fig. 2) we are using at present is a moderately flexible rubber covered applicator of flat coiled, stainless spring steel gilly wire with smooth blunt nickel steel ends each with a loop of stainless steel wire to facilitate attachment of the shoemaker's twine used in manipulating and holding the tandem in its proper position in the esophagus. It has an overall length of 12.5 centimeters although it is well to have a second and shorter applicator for the treatment of small lesions and those just below the level of the cricopharyngeal constriction. The radiation is produced by three radium element needles each of 10 milligrams strength. These needles have a filter of 0.25 millimeter of platinum and the total filtration of the applicator is equivalent to 0.4 millimeter of platinum. The radiation is 98 per cent γ and 2 per cent hard β.

Radon is not as satisfactory as the element because its radiation value would vary considerably over a 24 hour treatment period and frequent replacements would be necessary, thus leading to inadvisable handling and exposure by the clinicians and technicians. It is possible to vary the position of the radium needles in the container and so concentrate the dose by the use of two dummy needles as shown in Figure 2 A.

The stainless steel tube of flat gilly wire is flexible enough to allow the tandem to be readily drawn through the gastrostomy stoma and past the angle at the junction of stomach and esophagus. Its flexibility also facilitates its proximal extraction. The flat wire allows even radium filtration not possible when a round wire is used. This tubing is safe and is easily cleaned and does not rust and cause difficulty in the removal of the radium needles. The inside diameter of the tube is 1.5 millimeters—sufficient to allow easy introduction of the radium element needles. The outside diameter is 8 millimeters.

Securely screwed to each end of the flat wire tube is a smooth, blunt nosed, nickel silver piece which allows easy introduction without trauma through the gastrostomy stoma and also through the narrowed, diseased portion of the esophagus. Anchored in each of these end pieces is a short, nickel silver wire with a terminal loop to which is attached the strong twine used in manipulating the tandem. A section of ordinary black rubber tubing 8 millimeters in its outside diameter covers the flexible metal portions of the tandem.

The tandem is placed accurately in the esophagus at the level of the growth by combined gastroscopy and esophagoscopy. If the growth will permit the passage of a small (7 millimeter) olive tipped bougie, this is done under direct vision; otherwise the patient is given a black silk thread to swallow at the rate of a foot per hour for 24 hours. The gastrostomy stoma is gradually dilated with graduated Hegar cervix dilators and a small 9 millimeter esophagoscope is passed into the stomach, the gastric contents is aspirated, the organ is distended with air and the olive tipped bougie or string is picked up with biopsy forceps and brought out through the stoma (Fig. 3). Stout shoemaker's twine is substituted for the silk and tied to the tandem which is then passed through the gastrostomy stoma into the stomach and drawn upward into the esophagus to the lower level of the growth. The oral end of the string is then passed through a regular adult esophagoscope which in turn is inserted into the esophagus down to the tumor. By steady traction on the oral end of the string the tandem is pulled upward under direct vision until its proximal end is 3 centimeters above the upper limits of the disease (Fig. 4).

The esophageal lumen is usually quite narrow and the tandem tends to be held firmly in position

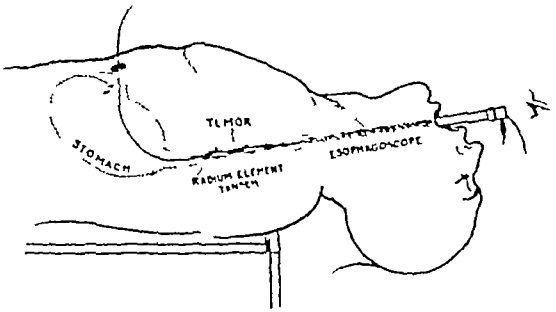

Fig 4 The radium element tandem is pulled upward by steady traction until, under direct esophagoscopic vision, the level of the esophageal lesion is reached

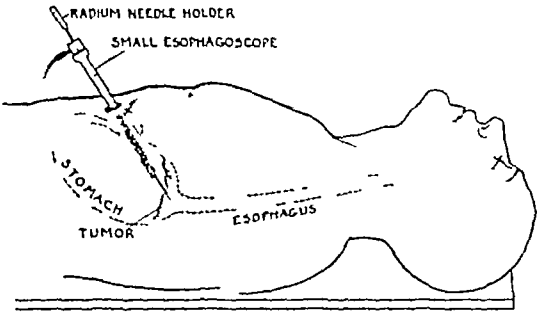

Fig 5 The method of inserting gold filtered radon seeds into a cancer of the cardiac portion of stomach by means of an esophagoscope inserted through the gastrostomy stoma

by the stricture, but it is nevertheless anchored in place by fastening the proximal end of string to a tooth and the distal end with adhesive tape to the anterior abdominal wall The length of the proximal and distal strings is measured and these measurements are used in reinserting the tandem for the next treatment, thus eliminating the necessity for repeated endoscopic procedures The tandem is left in position for 24 hours during which time the patient expectorates his saliva and regular nutrition is maintained by gastrostomy feedings

At the end of 24 hours, when a dose of 720 milligram hours (30 milligrams for 24 hours) has been delivered, the tandem is drawn upward and out through the mouth, a fresh length of string having been tied to the distal end and drawn through the stoma to be used in reinserting the applicator for the next treatment

The tandem is inserted every 2 days over a period of 8 to 12 days, during which time a total of from 2,280 milligram hours to 4,320 milligram hours is delivered to the tumor area The patients do not complain of discomfort during treatments, and if the throat is well cocainized and 1 per cent novocain is used to infiltrate the skin about the stoma before dilating it, they do not greatly mind the original endoscopic procedure and initial insertion of the tandem

Gastrostomy serves no useful purpose in cancers of the pyloric end and body of stomach, but it is of value in the inoperable lesions located in the cardiac portions of the stomach Growths in this latter region are apt to be difficult to diagnose roentgenographically, and on peroral endoscopy it may be impossible to visualize the growth or remove a biopsy In such instances the Janeway operation permits inspection of the growth and allows the operator to remove a specimen for microscopic diagnosis, at the same time he may measure the lesion accurately, estimate and insert the dose of gold filtered radon seeds necessary to control the growth (Fig 5) By weekly gastroscopy through the gastrostomy stoma the radium reaction may be followed and if regression is incomplete, check-up biopsies may be taken and more radon seeds added as necessary

If an esophageal lesion is to be treated by inserting radon seeds, it has been found a simple task with the aid of the esophagoscope to insert the radon seeds accurately into the upper two-thirds of the lesion, but, to plant gold seeds satisfactorily in the distal third of the growth, it is necessary to visualize this portion of tumor by retrograde esophagoscopy through the gastrostomy stoma For routine work in the esophagus and cardia of stomach, gold filtered radon seeds ranging in strength between 1 25 millicuries to 1 50 millicuries each have been found most satisfactory

Patients with cancer of the esophagus come to us at a late stage in their disease They are often quite emaciated and dehydrated, their tumors are large, ulcerated, and infected and frequently cause complete obstruction of the lumen (6) Many of these growths will shrink away and the esophageal lumens will open up under the divided dose method of treatment by external irradiation However, the beneficial effects of the radiation come on slowly—20 to 30 days after commencing treatment and, during this interval, the esophageal lumen is apt to become completely stenosed due either to esophagitis, continued growth of tumor, or the early initial hyperemic effect of the X-radiation In these cases it is necessary to do a gastrostomy before X-radiation is started, so that the treatment sequence will not be interrupted Later, when the tumor has re-

greased and the esophagitis has lessened, as it practically always will under external radiation, it is often possible to use the radium element tandem which previously could not have been inserted without excessive trauma to the growth

If an esophagectomy is planned, a preliminary gastrostomy should be carried out as the first step in the procedure and the Janeway type is here again most satisfactory for although much is written about the formation of a new anterior subcutaneous esophagus from loops of bowel, etc we have not seen or heard of a case in which such a procedure was productive of a satisfactory result and the rubber esophagus of Torek and Eggers when connected to a Janeway gastrostomy is still the most practical substitute for the normal viscus

Finally there is the occasional case which comes to us too late to warrant aggressive therapy yet the patient is aware of his prognosis and wishes for purposes of business, etc to carry on as long as possible In this group gastrostomy alone will prolong life and prevent death by starvation

SUMMARY

In cancer of the esophagus and cardiac end of stomach if a gastrostomy is to be done the Janeway type of operation is indicated because it possesses the following advantages

1 It allows the instrumentation necessary for the accurate implantation of gold seeds in the lowermost portion of an esophageal cancer and allows the safe retrograde insertion of the radium element tandem in the esophageal lumen at the site of the tumor

2 At operation or through the resulting stoma, it is possible to obtain a biopsy from a lesion located in the cardiac portion of the stomach and to insert gold seeds into it under direct vision and also to watch the ensuing radium reaction

(3) Retrograde bougienage for the dilating of a post treatment fibrotic esophageal stenosis may be safely carried out with graduated rubber dilators drawn through the mucous lined stoma

A gastrostomy is often necessary as a safety factor in cases of carcinoma of the esophagus selected for a course of X-radiation by the divided dose method

The operative technique of the Janeway gastrostomy is described in detail and a satisfactory radium element tandem for intra-esophageal irradiation is described together with the technique of its use

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PATHOLOGICAL FRACTURES DUE TO MALIGNANT DISEASE

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PATHOLOGICAL fractures due to malignant disease are common enough to warrant interest yet rare enough to make a statistical study difficult For this reason a wide diversity of opinion exists with regard to the prognosis Treatment is notoriously difficult and, all too frequently, unsuccessful Discussions of this subject are usually fragmentary, consisting chiefly of isolated case reports In order to clarify the subject we have studied the entire series of pathological fractures observed in the Pondville Hospital (the Massachusetts State Hospital for Malignant Disease) since its opening in 1927

HISTORICAL REVIEW

Thirty years ago surgeons regarded pathological fractures without hope Grunert, reviewing the literature from 1886 to 1904, stated, "We are justified in saying that in carcinomatous, that is to say, in true carcinomatous metastases, union of the fragments can never occur Up to this time there has never been a reported case of such a recovery" He believed that the prognosis was somewhat better in the case of osteogenic sarcoma "New osteoid tissue may be formed (in sarcoma), yet this seldom leads to a union At times a true union seems to take place and may exist for a considerable time" However, he cited 4 cases collected by Bruns and added 3 of his own cases that showed an early stage of union at autopsy

This impression prevailed for a decade thereafter Cotton, in 1911, said that fractures through carcinoma do not heal Bloodgood, quoted by Scudder, stated that union rarely followed fractures through metastatic carcinoma Codman agreed

Since then many reports have appeared in the literature of healed pathological fractures Kohler has reported several healed fractures through carcinomatous metastases Fractures through metastatic hypernephroma have been considered to be exceptionally resistant to healing, yet recently healed cases have been reported by Rypins and Gobbi Gobbi, in his article, has included abstracts of several other reports of healing of fractures through metastatic carcinoma of other types

As a result, the prognosis has been viewed more optimistically of late Pancoast, quoted by Ehason, believes that 40 per cent of cases of pathological fracture due to cancer heal In the same paper Sampson Handley is quoted as saying that union is the rule Ehason, however, emphasizes the poor prognosis, which he says is similar to that in sarcoma

Of 21 cases of bone sarcoma there were 2 cases in which Bloodgood found suggestive ossification One was his own, the other was recorded by Simmons Simmons saw partial ossification of the fracture by X-ray and in the amputated specimen Bloodgood thought much of the bone formation was associated with the neoplasm and not with the fracture

Coley reviewed 122 cases of osteogenic sarcoma from the Memorial Hospital There were 26 fractures—an incidence of 21 per cent In this series union occurred in none There were 36 cases of endothelial myeloma, of which 26 per cent (9 cases) showed fractures Union occurred in 3

The wide disparity of views with respect to healing through metastatic carcinoma is difficult to understand unless such impressions have been based upon an insufficiently large series of cases That such cases are comparatively rare is attested by MacDonald's figures He reviewed the fractures of the long bones observed in the Massachusetts General Hospital for a period of 10 years (1910–1920) During this period 1 045 fractures were treated of which 24 were pathological Three of these cases occurred through metastatic carcinoma, 3 through sarcoma

THE X-RAY AND THE PATHOLOGICAL FRACTURE

It has long been a disputed question whether or not X-ray treatment is indicated in the treatment of a pathological fracture Unfortunately it is impossible to obtain any experimental data, derived from animal study, on this problem In a pathological fracture healing is not as simple as in an ordinary fracture Tumor cells, when abundant and proliferating rapidly, interfere markedly with the formation of callus Relatively speaking, the amount of osteoblastic tissue available for repair is greatly reduced Proponents of the use of X-ray point out that it is necessary to kill those malignant cells in order to allow adequate room for bone repair to proceed Opponents of the use of X-ray believe that its use will impede the proliferation of connective tissue and osteoid deposition

There is no reason to suspect that the process of repair of a pathological fracture varies from that following a simple fracture except in so far as the malignant tissue present tends to slow the repair For this reason it should be advantageous to review the experimental work done on the relation of X rays to healing of simple fractures.

Perthes observed in 1903 that if a fowl s wing was treated with X-ray it lagged behind in development. Similar retardation of the growth of young bones was reported in guinea pigs by Trebondeau and Recamier

Working with fractured radii in rabbits, Salvetti found that after large doses of X ray (the accurate doses are not given) the bone trabeculae were smaller than normal, the cartilage cells were frequent, and the calcium salts were deposited more abundantly He believed this increased deposition of calcium was not a sign of good callus formation, but an attempt of the body to compensate for the thinness of the trabeculae.

Churet irradiated femora of dogs both before and after setting the fractures. He found a diminution of the amount of callus formation. Muller resected sections from the radius in rabbits. He could find no callus stimulation from small doses of X-ray and believed that they retarded growth.

Fraenkel, in 1914 was the first to ascribe an effect of callus stimulation to the X ray He found a considerable shortening of the time of healing in many complicated fractures after irradiation. Kohler in a clinical study of 87 fractures, found that a light X-ray treatment usually more than halved the time of repair Krynski, Carrando, Ottolenghi, and Tammann all report beneficial effects from X-ray treatment. Tammann employed 25 per cent of the skin erythema dose on fractures of the tibia in rabbits The irradiated fractures showed considerable advance in healing in 5 days. After 30 days the repair was still slightly better in the irradiated group Turco confirmed these findings

Latten conducted experiments on fractures of the coccyx of rabbits. He irradiated with X-ray varying from 10 to 90 per cent of the skin erythema dose and examined the fractures microscopically each 5 day period for 30 days He could find no indubitable evidence of callus stimulation from X-ray But he could find no ill effects arising from light, moderate, or heavy doses of X ray on healing He found that healing proceeded so irregularly in different animals that it was hard to evaluate the effect of radiation He criticizes previous clinical observations, believing that factors such as age size, and nutritional state are much more important factors than the presence or absence of X-ray measures. Fujanimi has pointed out that fracture healing in various animals proceeds differently This may explain some of the discrepancies observed by investigators employing different animals. It also throws some doubt on the applicability of any conclusions gained from animals to man.

Fukase experimented with fractured fibulas of rabbits. He fractured both tibias of 84 rabbits, irradiating one side of each animal immediately after the fracture. The other side was used as a control. Because of the splinting furnished by the tibiae, the fracture lines were not subjected to unequal forces, such as was the case in many previous experiments. Individual variations in healing were also eliminated in his experiment since both irradiated fracture and control occur in the same animal

He employed extraordinarily high doses of X ray in the first experiment. He gave doses of 400r each on four successive days. There were used 170 kilovolts with a 0 5 millimeter zinc filter Each dose required 15 minutes, and corresponded to 75 per cent of a skin erythema dose. He found that while calcium was deposited in the control fractures in 2 weeks it required 3 weeks after this heavy irradiation Histologically, for this length of time the irradiated areas were filled with a thin connective tissue, the cells of which resembled bone cells After 3 weeks numerous vessels appeared and calcium was deposited rapidly

A series of fractures was then studied using a single dose of 400r These fractures developed less callus than the normal, while calcification set in earlier and was more rapid than without irradiation. With 200r doses a clear effect on the course of healing could not be recognized

In summary of the relation of irradiation to fracture healing, it may be concluded that small doses of X ray produce no significant change, large doses retard healing and moderate doses, i e about 400r in the hands of most observers, have been shown to accelerate healing

Therefore there seems to be no contra-indication to the use of the X-ray in pathological fractures provided that only moderate doses are employed Not only is healing stimulated, but the amount of malignant tissue interfering with repair is diminished

Several case reports appear in the literature of pathological fractures treated with the X ray Kohler had 2 cases The first was that of a 51 year old woman who had a carcinoma of the breast. There was an extensive metastasis in the neck of the femur with involvement of the skin and with pathological fracture Four erythema doses were

given to the femur at intervals of 1 month The radiation field was 18 by 14 centimeters at a distance of 50 centimeters One hundred ninety kilovolts with a filter of 0 5 millimeter zinc and 3 millimeters of aluminum were used There was healing in 5 months His second patient, 18 years of age, had a metastasis in the humerus, with fracture, from a lymphangio-endothelioma of the sole of the foot Three erythema treatments were given at intervals of a month There was healing 3 weeks after the first treatment

Rypins' case was a man of 46 who had 2 fractures through metastases from a hypernephroma One fracture through the ulna was given an X-ray treatment of 10000 (200 kilovolts, 4 milliamperes, filtration 2 0 millimeters copper, 1 0 millimeter aluminum, field 10 by 15 centimeters) The other through the tibia received no treatment Both fractures showed healing 5 months later

OTHER METHODS OF TREATMENT

Various other methods of treatment of fractures have been suggested They include the injection of calcium and phosphorus (Albee and Morrison, Haldeman and Moore), excess intake of vitamin A, and the development of acidosis Mettenleiter has irradiated the thymus of rats and claims more rapid healing of fractures results We have not been convinced of the value of any of these procedures and have not employed them

Irradiation of the ovaries, as shown by Dresser and others, frequently leads to bone deposition in metastases from carcinoma of the breast Sterilization has been employed in nearly all cases of recurrent and inoperable cancer of the breast in this hospital We have recently begun to sterilize nearly all premenopausal patients with mammary carcinoma

PONDVILLE CASES

This study comprises all the pathological fractures which have been observed in the Pondville Hospital from its opening in 1927 through December, 1934 It is necessary to define the term "fracture" as employed in this paper The usual definition of a fracture is a solution of continuity of a bone In an academic sense, therefore, every metastatic area in bone is a fracture Cases are not rare in which nearly the entire shaft of a bone, so far as can be determined by X-ray, has been replaced by metastatic disease Yet the limb clinically shows no localized tenderness and no displacement These cases have been eliminated, only those cases are included in which a fracture line was distinguished by X-ray, and found to be associated with bone destruction characteristic of a metastatic or primary tumor

TABLE I —SOURCE OF PRIMARY TUMOR

	Number	Per cent
Breast	26	49
Lip, mouth, etc	11	20
Prostate	6	11
Osteogenic sarcoma	5	10
Cervix	2	4
Thyroid	1	2
Liver	1	2
Kidney	1	2
	53	

During this period, there have been 4,739 cases of malignant disease admitted to the hospital There have been 66 fractures in this group, occurring in 53 patients Only those fractures in which the evidence clearly pointed to previous malignant disease of the bone are included This eliminated several fractures through decalcified bone in patients in a poor state of nutrition Also eliminated are several fractures occurring through areas involved by Paget's disease Finally those cases in which the fractures were first discovered on the postmortem table are not included since there is no positive proof that the fractures were present before death

TYPE OF TUMOR

The primary sources of the tumor are listed in Table I Carcinoma of the breast furnishes the largest number of fractures During these 7 years 637 cases of cancer of the breast were admitted to this hospital Of this number 151, or 24 per cent, had osseous metastases Twenty-six patients, or 17 per cent, showed fractures Geschickter and Copeland found that fractures occurred in 15 of 100 cases of carcinoma of the breast with bone metastases Carcinoma of the tongue, lip, floor of mouth, and buccal mucosa frequently involve the mandible by direct extension Rarely they metastasize to other bones Cancer of the prostate, of which 161 cases were admitted, showed 78, or 48 per cent, with osseous metastases, but only 8 per cent of fractures This relatively lower percentage compared with cancer of the breast is due to the hyperplastic character of most prostatic metastases

Fractures through osteogenic sarcomas are relatively frequent but usually occur late in the disease It is unusual that we have had only one fracture through a metastatic hypernephroma There have been 30 cases of renal cell carcinoma observed here, of which 6 had osseous metastases

BONES INVOLVED

The bones involved are shown in Table II. Of those fractures occurring in the femur, 2 were in

the mid-shaft, 1 in the lower third (through an osteogenic sarcoma). Of the remainder approximately half were in the neck of the femur, the others in the upper third. Only 2 were subtrochanteric. Of those in the humerus, 3 were found in the surgical neck, 1 in the lower shaft, and the remainder in the upper third of the shaft.

Sixteen fractures, or 28 per cent, were found in the flat bones. Considering the large number of metastases that are found in the vertebral column it is remarkable that fractures are seen so rarely. The vertebræ collapse and mushroom frequently but a true fracture line is extremely rare. Only those cases with a fracture line are included.

PROGNOSIS

It is difficult to evaluate the prognosis after a pathological fracture. Coley believes that the life expectancy of a patient with osteogenic sarcoma through which fracture has occurred is shortened 60 per cent. While theoretically the presence of a fracture should shorten a patient's life we feel that the majority of such fractures occur in cases of advanced disease, and that it is difficult to prove that a fracture, per se, shortens life.

In our series 25 per cent of the patients died less than a month after the fracture. Approximately 25 per cent died in the next 2 months, and another quarter before the expiration of a year after fracture. Eight patients are still living one 3 years after fracture (#3448—history below), and another 2 years after fracture (#5828—v.i.). Three other patients are living 6 to 8 months after fracture occurred.

The average duration of life after all fractures including cases that are still living is slightly over 6 months. If the carcinomas and sarcomas are separated, the prognosis with respect to length of life is seen to be nearly twice as good in the latter group. In this group the average life was slightly more than a year after fracture, while in carcinomas it was slightly less than 6 months (Table III).

TABLE II.—SITE OF FRACTURE

	Number
Femur	29
Humerus	1
Mandible	
Pubis	6
Clavicle	4
Rib	
Vertebra	
Tibia	
Ulna	1
	66

TREATMENT

Many of our cases had no specific fracture treatment. This group included, for the most part, those cases in which the fracture was first discovered on routine X-ray examination and in whom there had been no signs or symptoms of fracture. Asymptomatic fractures are relatively common.

In patients with advanced disease, union is so rare that the maximum effort should be directed to making the patient comfortable rather than to securing exact anatomical position. Light traction—about 10 pounds for fractured femora—usually contributes to comfort. More than this weight is usually contra-indicated because of muscular atrophy. Sandbags are occasionally tolerated when traction is unbearable.

Certain cases have a minimum of metastatic disease but receive a fracture. It is in this group that attempts must be made to secure solid union in as short a time as possible. Various types of orthopedic appliances have been employed. We have found a modified Buck's extension to be valuable in the treatment of a fractured femur. Lund swathes are used in fractures of the humerus. We have not attempted surgical manipulation under anæsthesia in any case because of the great danger of increasing the deformity. Walking caliper splints are valuable not only for convalescent fractures, but also as preventive devices to be employed in known metastatic disease before fracture occurs.

What is the value of X-ray in the treatment of these fractures? Reference to Table IV indicates that it was employed in only 3 cases of fracture of the femur, 2 cases of fractured humerus, 1 of fractured mandible, and 1 of the pubis. It is necessary to analyze the subsequent progress of these patients in order to see whether or not healing is more satisfactory in this group.

The healing of a fracture may be judged by several criteria. Opportunity has been given to examine many of these fractures after death; absence of the fracture at postmortem is satisfactory evidence of healing. Disappearance of the fracture line by X-ray provided that there has not

TABLE III.—PROGNOSIS

	Number
Died less than 1 month after fracture	10
Died 1 to 3 months after fracture	1
Died 3 to 6 months after fracture	0
Died 6 to 30 months after fracture	3
Living	3
Data incomplete	9
	31

Fig 1

Fig 2

Fig 3

Fig 1 L C Case 5828 February 27, 1933 There is an extensive destructive process involving the right mandible with pathological fracture

Fig 2 L C Case 5828 This roentgenogram which was taken November 23, 1933, shows that the pathological fracture has united and that there is regeneration of the areas of destruction

Fig 3 L C Case 5828 March 7, 1935 There is firm union at the site of the pathological fracture and no evidence of disease

been progressive destruction of the fragments by malignancy, is indicative of healing On the other hand there are many fractures which, after a period of time, show only partial healing by X-ray They may have little evidence of new bone or callus formation, but the patients have extremities that can be moved without pain or crepitus This group we style "fair healing" Some cases have a useless extremity but show slight X-ray or autopsy evidence of healing, this group shows "slight healing" Many cases show no signs of healing

Of our 65 fractures only 3 (5 per cent) healed These cases all showed firm union, comparable to that following a simple fracture Of these, 1 was a fracture of the mandible which received heavy irradiation

CASE 6828 L C This 61 year old man entered the hospital February 26 1933 complaining of an ulcer of the cheek of 6 weeks' duration He had an epidermoid carcinoma, grade I of the buccal mucosa of the right cheek There was extensive thickening continuous with the carcinoma extending over the right jaw and into the submaxillary region The admission diagnosis was carcinoma of the

TABLE IV —TYPES OF TREATMENT

Type of treatment	Mandible	Femur		Humerus	Pubis	Clavicle	Rib	Vertebra	Tibia	Ulna
		Ca	Sa							
No treatment	2	4	1	-	5	1	2			1
X ray only	8	1			1					
Traction		9	2							
Cast		3							1	
X ray and cast		1								
X ray and traction		1								
Sandbags		1								
Splint		1				2				
Amputation			1							
Swathe				3						
X ray and swathe				3						
Thomas collar								1		
Not stated		3	1	3		1	1			

Fig 4

Fig 5

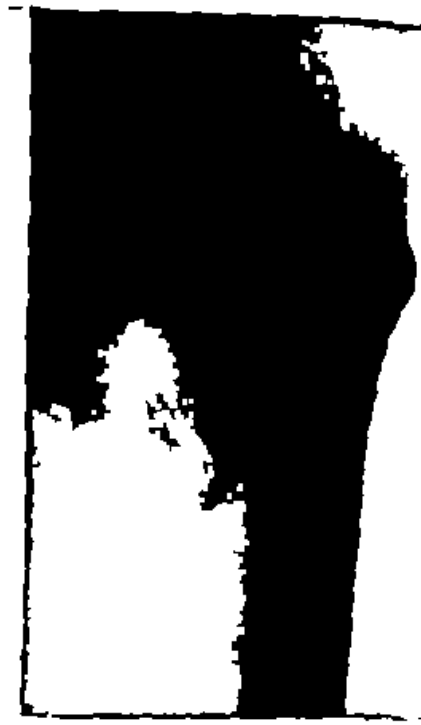

Fig 6

Fig 4 C J Case 204 December 15, 1927 There is mottling and rarefaction in the upper end of the femur There is an intertrochanteric fracture, with no displacement.

Fig 5 C. J Case 204 May 3, 1928 Only the extreme upper end of the fracture line is visible Areas of rarefaction are much less prominent

Fig 6 C. J Case 204 September 27 1928 Fracture is well healed There is extension of metastatic disease in the head and neck

bucral mucosa with metastases [illegible] the neck. X ray examination by Dr Dresser was reported to show an extensive destructive process on the right side of the mandible with pathological fracture The changes are indicative of malignancy"

He was given 2400 units of X-ray to the right face and neck (5 by 15 cm. field, 200 kv to mm, 50 cm distance time 4' min w l 0 160, filter 4 mm Cu, 5 mm Al) He developed marked X ray reaction On May 4 the intraoral ulceration had disappeared The X-ray report on this date was comparison with previous films shows slight enlargement in the defect of the anterior portion of the ramus, but outlines of the bone are definitely smoother

On May 6 an additional 1200 units of X ray were given to the right face and neck On November 3, 1933, a film of the jaw showed complete union of the bone of the pathological fracture and regeneration of the region of destruction The lesion of the jaw has now completely healed over There is union of the fragments of bone and regeneration of the areas of destruction

On March 7 1935 there was no evidence of disease

The second case was a fractured humerus which was found to be healed at autopsy

Case 20 H C This 55 year old woman entered with carcinoma of the breast There were fractures of the left femur and right humerus, believed to be of 7 weeks duration A splint was applied to the arm and traction to the leg X ray 8 weeks after admission was read as follows

Film of the right shoulder shows a fair amount of bony callus in the region of the fracture The entire upper portion of the humerus is absorbed by tumor The fracture of the left femoral neck shows very little bony union

At autopsy 6 weeks later "the upper portion of the right humerus was removed and showed pathological fracture with firm union The upper portion of the left femur was also removed, which also showed a pathological fracture and rather fibrous union X ray treatment was given to this patient.

The third case was that of a fractured femur

Case 204 C J This patient, when 45 years of age, had radical mastectomy for scirrhous carcinoma in July 1924 She developed fracture of the right femur in November 1927 She was kept in traction for 5 weeks and then plaster spica was applied In December 1927 the X ray treatment were given centered over the anterior superior spine and the posteriorly at the same level (Each was given over a 20 by 20 field, 200 kv 5 mm 25 mm 30 cm distance filter 2 mm Al, 0 5 mm Cu)

The cast was removed in February 1928 Soon after 2 treatments similar to those outlined were given, 1 anteriorly and posteriorly As X ray film at this time showed increased calcium deposition In May 1928, she was walking with a cane By X ray only the extreme upper end of the fracture line was visible In August, 1928, 4 more X ray treatments were given, 2 anteriorly and 2 posteriorly to the region of the fracture A similar course was repeated October 1928 Her last X ray was on September 7 when the fracture line had healed, but there was increase in the amount of the metastases In November 1928, she was discharged with walking caliper splint She died September 1929 at home

In the group that showed fair healing there were 6 cases (9 per cent)

Case 3392 C W This 8 year old woman entered the hospital in November 1932 complaining of pain in the

Fig 7 Fig 8 Fig 9

Fig 7 M M Case 8705 January 12, 1935 There is diffuse metastatic disease in the upper half of the humerus A pathological fracture of the surgical neck is present

Fig 8 M M Case 8705 January 22, 1935 The medial displacement of the lower fragment is more marked There is no evidence of callus formation

Fig 9 M M Case 8705 February 18, 1935 There is a moderate amount of callus present Union is firm clinically

left hip of 3 months' duration The X-ray report at this time was "The intertrochanteric region, head, and neck of the left femur show mottled bone destruction with considerable new bone formation There is evidence of new bone extending into the soft tissues There is apparently a spontaneous fracture through the neck of the femur" 8oor units of X-ray were given both anteriorly and posteriorly over the fracture. (15 by 15 field, 10 ma, 200 k v, 4 mm Al, 0 5 mm Cu filter, 200r per treatment.)

In January, 1933, the fracture line was no longer visible At this time the left hip was ankylosed at 45 degrees During the next 6 months the patient's liver gradually enlarged and she developed ascites Three months before death 600r of X-ray were given over the left hip, anteriorly Death occurred in July, 1933 At autopsy a bile duct carcinoma metastatic to the left femur was found The autopsy report read "The region of the trochanter, neck, and head of the left femur are occupied by a tumor mass, involving the soft tissues and the ilium It is firm in consistency and on section is yellowish white in color It contains a large amount of new bone formation"

Case 3448 S Y In November, 1930, this 30 year old woman sustained a fracture of the lower end of the femur through what was believed to be a bone cyst A plaster cast was applied She was first admitted to this hospital in June, 1931 At this time the patient was walking with a slight limp, because of slight pain on weight bearing X-ray showed "an extensive pathological process involving the supracondylar area of the left femur The cortex is broken on both sides of the bone Apparently there is a spontaneous fracture." Amputation was done in August The specimen was described as follows ' The medullary cavity at the epiphysis of the femur is filled with a friable, gray green material, and the edges of the cavity are replaced by tumor tissue The periosteum is intact except in one portion where there is a recent, irregular fracture with a moderate amount of callus and bone formation Microscopically pleomorphic spindle shaped cells closely packed are found Atypical and typical mitoses are very numerous There is a moderate amount of hemorrhage and necrosis Diagnosis osteogenic sarcoma (fibrosarcoma) " The patient was alive and well November 21, 1934, without evidence of recurrence

This patient had no X-ray treatment.

Case 248 L W This 44 year old woman entered the hospital 18 months after a mastectomy for carcinoma X-ray showed multiple bone metastases She received 2 X-ray treatments, 1 over the left sciatic notch, and 1 over the left lower femur, these treatments were given 2 weeks after she complained of severe pain in her left hip (Treatments were given over a 20 by 20 field, 50 cm distance, 200 k v, 5 ma, filter 0 5 mm Cu, 2 0 mm Al.)

Two months later by X ray "the upper end of the femur at the level of the lesser trochanter showed definite outward bowing with evidence of a fracture that has apparently been healed No trace of this was visible at the previous examination" The patient was kept in bed 2 months She then rested weight on her left femur, and it snapped at the site of the old pathological fracture The leg was then put up in traction Four months later X ray showed lateral displacement of the upper fragment She died 11 months after entry

Case 8352 G K In 1932 this 49 year old woman had X-ray treatment for a carcinoma of the breast. She en-

Fig. 10 Fig. 11 Fig. 12

Fig. 10. J. F. Case 8088. October 30, 1934. There is extensive bone proliferation in the upper part of the left femur and pelvis, combined with some areas of destruction. There is a transverse fracture of the shaft just below the trochanters.

Fig. 11. J. F. Case 8088. January 4, 1935. There is a moderate amount of new bone formation. Fracture line is clearly visible.

Fig. 12. J. F. Case 8088. February 8, 1935. There is now considerable new bone formation. The fracture line is indistinct but still present.

tered this hospital August 31, 1934, with a pathological fracture of the upper end of the shaft of the right humerus. 2000 units of X ray each were given, centered over the anterior and posterior surfaces of the right shoulder joint (20 by 20 cm. field, 200 k. v., 5 ma., 50 cm. distance, 4 mm. Al., 0.5 mm. Cu filter, 4000 each treatment.)

X ray on November 8 showed new bone forming by the fracture. In February, 1935, the right arm was practically useless although there was apparently firm union in a bad position. X ray examination, however, revealed no change since the previous examination.

Case 8705. M. M. This patient entered this hospital in November, 1934, when she was 63 years of age. She had had simple mastectomy for carcinoma in 1930. Recurrences had been removed twice thereafter. A breast series was negative on entry. The patient had numerous recurrences along the scar. A radical mastectomy was done. Two months afterward the patient began to complain of pain in the right shoulder and shortly afterward received a fracture of the surgical neck of the humerus. The patient had received 3000 units of X-ray daily, directed over the posterior surface of the right shoulder joint, on the 3 days preceding and including the fracture (5 by 5 cm. field, 20 ma., 200 k. v., 50 cm., 0.160 w. l., 4 mm. Al., 3 mm. Cu filter.)

After 3 weeks treatment by means of Lund swathe bone there was no evidence of new bone formation. 6000 units of X ray were then given to each of the anterior and posterior surfaces of the right shoulder. The patient was discharged about 7 weeks after fracture. By X ray there was evidence of a small amount of new bone formation. The arm could be moved without pain and there was no tenderness. Patient reported to the clinic in September, 1935. At this time bony union was present, although there was still marked irregular thickening of the upper end of the humerus.

Case 4418. G. W. J. July, 1926, that 36 year old woman received X ray therapy elsewhere for carcinoma of the breast. In March, 1928, she sustained pathological fracture of the left femur. She was placed in plaster spica. She first entered this hospital in April, 1928. On June 1 there was a fracture of the surgical neck of the right humerus, through an area of metastatic disease. On August 9 an X ray film of the hip showed no visible callus formation. At this time the patient had good use of her right arm and, clinically, firm union at the site of the fracture. No X rays of the humerus were taken, however, after the metal plate. The patient died in December, 1928. No autopsy.

In the group that showed slight healing there were 4 cases (6 per cent.)

Case 20. H. G. History has been given.

Case 8316. M. S. This 67 year old woman entered the hospital nearly moribund, with carcinoma of the breast metastatic to skull, vertebra, pelvis, and lung. X ray showed an old pathological fracture of the left femur with evidence of slight healing. N. treatment was given. She died 6 days after entry. There was no autopsy.

CASE 5088 J P This man of 75 years was admitted to the hospital with a pathological fracture of the left femur subtrochanteric in October, 1934 His prostate was moderately large and firm with thickening about the left upper pole Hyperplastic metastases were visible in the left femur and ilium Buck's extension with 10 pounds traction was applied Two months after fracture the patient could stand for a few moments on his leg At this time there was a large amount of new bone formation but the fracture line was still visible In February, 1935, the fracture line showed no healing but the fracture was firmly united to palpation At this time the patient was discharged against advice having been confined to his bed for the past month

CASE 3442 A P This 61 year old man entered in January 1931 with acute retention He received radium implantation and suprapubic cystotomy for carcinoma of the prostate He received X ray therapy to the pelvis He sustained a fracture of the upper end of the shaft of the left femur in June 1932 He was placed on Buck's extension An X ray in October 1932 showed angulation and overriding of the fragments but considerable new bone formation At this time the union was firm clinically However, the patient never got out of bed after the fracture He died in February 1933 At autopsy the fracture was still present.

SUMMARY

In 53 cases (80 per cent) we obtained no evidence of healing

The methods of treatment may be summarized as follows In the cases with satisfactory healing one had heavy X-ray alone One case had fixation and X-ray in moderate dosage One had fixation alone In the 6 cases with fair healing 2 cases 1 of which was an osteogenic sarcoma, had fixation only Three had a moderate amount of X-ray, in 2 of these cases it was combined with fixation One had a small amount of X-ray with no other treatment Of the 4 cases that showed slight healing 3 had traction only 1 case had no treatment in this hospital None had X-ray for treatment of the fracture

Of the 52 cases that did not heal, 8 received X-ray treatment with no benefit These cases included 1 fracture of the pubis, 7 of the mandible It should be noted that fractures of the mandible form what should be considered a distinct group They are compound fractures, all grossly septic Moreover, there is frequently wide separation of the bony fragments They are therefore the most resistant of all fractures to treatment

A question of great importance is whether or not X-ray treatment of a bone metastasis is of any value as a prophylactic against fracture We have treated only an occasional case before fracture, so at present are unable to advance any data on the problem

Other factors than X-ray treatment are of course of great importance in the prognosis of fractures The condition of the patient must be considered The best results may be expected in patients who are in good general health and who have a single bony metastasis

CONCLUSIONS

1 Sixty-six pathological fractures occurring through carcinoma or primary osteogenic sarcoma are reported

2 Experimental study reviewed shows that treatment of a simple fracture with moderate doses of X-ray accelerates healing

3 Five per cent of our fractures healed with firm union Nine per cent showed moderate healing Six per cent healed slightly No evidence of healing was obtained in 80 per cent

4 Of our 9 fractures that healed, either fully or moderately, 6 cases received X-ray therapy to the bone after the fracture

5 In our series the average length of life following fracture through carcinoma was slightly less than 6 months After fracture through osteogenic sarcoma, the length of life averaged slightly over a year

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LYMPHOPATHIA VENEREUM—"LYMPHOGRANULOMA INGUINALE"—OF THE FEMALE URETHRA

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CHRONIC inguinal adenitis, frequently progressing to suppuration with multiple draining sinuses, occurring chiefly in men and only occasionally in women, has been described for over half a century and under many names Durand, Nicolas, and Favre described the condition in 1913, realizing that it was not a new disease and that it had been portrayed by many previous authors Their work served to draw attention to this clinical entity They proposed the name "lymphogranuloma inguinale," thinking the microscopical picture was similar to Hodgkin's disease Unfortunately, this confusing term has since then been widely used, although it has been clearly demonstrated that there is no relation or real similarity to Hodgkin's disease While the disease was studied by many investigators, no great progress was made until Frei (9), in 1925, discovered a specific diagnostic antigen prepared from the bacteriologically sterile pus[1] from these cases His intradermal test gave impetus to worldwide studies The disease has been transferred to monkeys and mice (Hellerstrom and Wassén, Levaditi, Ravaut and Lépine, Findley, and others), producing a characteristic meningitis after intracerebral inoculation, to guinea pigs (Meyer, Rosenfeld, and Anders), producing a typical inguinal adenitis after inoculation in the groin, and to other animals The filterable virus nature of the causative agent has been made clear by a number of investigators (Hellerstrom and others) Recently, Tamura claimed to have cultured the virus, using special media, and to have reproduced the disease in guinea pigs from the cultures "Lymphogranuloma inguinale" is now generally accepted as a proved disease entity

By means of the Frei test several other interesting clinical conditions have been linked with "Lymphogranuloma inguinale" The association of large labia with ulceration of the skin and vaginal mucous membrane, hypertrophic tags about the rectum, and sometimes with rectal stricture, has been recognized for very many years The terms elephantiasis vulvæ, esthiomène, chronic hypertrophic vulvitis, and genito-ano-rectal syndrome have been used to indicate this disease It was perhaps due to Fournier who in 1875 gave the name "anorectal syphiloma" to the hyperplastic infiltration which leads to stricture of the rectum, that syphilis has been most widely considered the cause of this syndrome Not only syphilis, but tuberculosis, chancroid (Ducrey infection), gonorrhea, and, in more recent years, granuloma inguinale have been ascribed as causes in a most extensive literature The development of knowledge concerning granuloma inguinale made it clear that syphilis and other conditions mentioned were rarely, if ever, the cause of esthiomène For a period of years it was thought that all cases were due to granuloma inguinale Some contemporary authors have considered that esthiomène is due to a combination of diseases and local injuries (Stein, Taussig)

Since 1928 when Frei and Koppel (11) first reported positive Frei tests in a small series of patients with esthiomène and rectal stricture, numerous other publications have appeared in support of the "lymphogranuloma inguinale" virus as the cause of these conditions (Bartels and Biberstein, De Wolfe, Lee and Staley, and others) Bartels and Biberstein have given their interpretation of the pathogenesis, showing that the infection has an especial tendency to involve the lymphatics

They believe that the predominance of rectal stricture in women is due to the fact that the lymphatics of the posterior wall of the vagina and the fourchette drain to the subperitoneal surface of the rectum where they join with the lymphatics coming from the rectal submucosa Such an explanation, however, involves the assumption of a retrograde transport of the virus through the wall of the rectum into the submucosa, where the oldest and most prominent lesion of rectal stricture is found It is possible that this could be effected by progressive septic thrombosis of the lymphatics The more common location of the lesion in the ampulla is attributed to the unusually rich mucosal lymphatics in this region

A proper understanding of the clinical forms of this virus disease has been difficult because of the unfortunate name "lymphogranuloma inguinale" The disease is confused with Hodgkin's disease, commonly called "lymphogranuloma," but which has no known relation to the condition under

[1] The use of pus as an antigen has certain disadvantages Grace and Suskind (Proc. Soc Exper Biol. & Med 1934 32 71) have advised the use of a mouse-brain antigen. It is likely that such a preparation from infected animal material will prove more satisfactory than the original Frei antigen

consideration. It is also confused with granuloma inguinale a quite different disease primarily affecting the skin and caused by Donovan a organism "Lymphogranuloma inguinale as shown by the Frei test, is by no means limited to the *inguinal region. However several authors have* demonstrated that the inflammatory reaction characteristically extends along and blocks the lymphatics. Its venereal nature has been alluded to by many Wolfe and Sulzberger propose the name lymphopathia venereum an apt, clear distinguishing and descriptive term and one that *will hereafter be used in this* paper

The purpose of this paper is to present a series of 11 cases which seem to indicate the stages of a syndrome occurring in women beginning with a chronic urethritis and progressing to urethral stricture or extensive urethral ulceration. Nine of the 11 are associated with positive Frei tests

Chronic abacterial urethritis, in which no bacteria could be cultured or could be ascribed as a cause was perhaps first described by Waelsch in 1904. *So far as we know his work and this condition have received no recognition in this country*

Curth in 1931 described a male patient with enlarged inguinal lymph nodes and urethritis. A smear of the discharge from the urethra showed leucocytes but no bacteria. The patient himself showed a positive Frei reaction, and an antigen *prepared from the urethral discharge acted as a* specific Frei antigen. In 1932 Frei (10) reported a case of chronic abacterial urethritis in a young man with negative Frei test. However an antigen prepared from the urethral discharge did act as a specific antigen when injected into patients with known lymphopathia venereum. But the discharge when *injected into a monkey did not pro*duce the typical encephalitis Kalz (14) in 1933, presented 3 patients with the Waelsch type of urethritis with negative Frei tests From the urethral discharge of each an antigen was prepared, which acted similarly to known Frei antigen. There has been some discussion of the cases *of Frei and Kalz, as to whether the original pa*tients had anergy whether the lesion was too superficial to produce allergy or whether the urethritis in these cases was due to a virus which was different from but closely akin to that of lymphopathia venereum Polak (1933) described 3 carefully selected cases in which an abacterial urethritis was associated with *large inguinal lymph* nodes and positive Frei reaction Berecny (1934) presented another case of chronic non-gonorrheal urethritis with strongly positive Frei test and the specific antigen was recovered from the urethral discharge All of these patients were men

Various ulcerations of the vagina have been reported as associated with esthiomene or rectal stricture and with positive Frei reaction These ulcerations have been found more commonly about the fourchette Richter (1932) described an extensive ulceration of the entire anterior vaginal wall with a smaller ulceration in the fourchette, occurring in a woman of 25 years The urethra was not mentioned as being involved The Frei test was positive. The patient also had syphilis, but intensive anti syphilitic treatment had no effect on the lesions.

Weissenbach Martineau, and Fourestier (1934) reported the case of a 44 year old woman with rectal stricture, urethral infiltration, and incontinence of urine. The interior of the urethra was edematous, congested and there was a false purulent membrane. The Frei test was positive Serological tests for syphilis were negative. This is the only report in the literature of involvement of the female urethra of which we are aware

CASE REPORTS

CASE 1 F J The patient, negro female of 41 years, as first seen in 1934 complaining of a ere burning and straining on urination with nocturia (2 times a night) *for 3 months* 1 to 3 years previously her physicians told her she had inflammation of the womb and bladder For 3 years she had had urgency of urination and had been occasionally incontinent The uterus was three times normal size There was slight pyuria Bladder cultures showed on one occasion few colonies of Bacillus coli, on another Staphylococcus albus Hysterovaginectomy was done but with no relief of the bladder symptoms In 1935 the external genitalia were normal, the cervix normal and well suspended, and no rectal lesion was found The inner part of the urethral meatus was slightly injected No purulent material could be expressed Urethroscopic examination showed marked injection along the course of the urethra but no ulceration The bladder appeared normal Repeated cultures showed no growth Repeated Wassermann tests gave negative reactions Local applications of silver nitrate gave no benefit Frei reaction was positive After more than 1 year of treatment, the patient remained no better

CASE 2 D B The patient, negro female of 29 years, was first seen in 1934, complaining of diurnal urinary frequency every 3 minutes, and nocturia 5 to 6 times beginning 3 days previously There was occasional incontinence some dribbling, and slight dysuria There years previously because of a positive Wassermann reaction, she was given doses of diarsenol and 10 of bismuth in another clinic Examination showed no palpable inguinal glands, normal external genitalia, and negative pelvic and rectal findings A small point like projection was found on the posterior margin of the urethral meatus, which looked like wart and had the appearance of normal vaginal tissue There was definite obstruction at the junction of the internal urethra and bladder On the right side of the internal urethra near the junction with the bladder definite ulcer triangular in shape was found which bled freely The bladder and trigone appeared normal Numerous cultures showed only varying organisms which are constantly considered contaminants The stricture was gradually dilated,

and silver nitrate 3 per cent and gomenol were applied to the urethra In 1935 after many treatments the symptoms showed little or no improvement The urethra was diffusely injected and granular Repeated Wassermann reactions were negative Frei reaction was positive During a year of treatment the symptoms were improved at one time but soon returned and showed no improvement

CASE 3 C H The patient a negro female of 43 years, was first seen in 1931 complaining of dysuria and straining on urination It began 3 years before, with marked frequency and nocturia 10 times Twelve years previously she had had a sore on one labium and 7 years before she had 12 intravenous injections at another hospital On examination the external genitalia were normal The posterior wall of the anterior two-thirds of the urethra was missing but there was apparently no fresh ulceration In addition there was a marked stricture in the region of the internal sphincter There were myomata uteri Rectal examination was negative Cultures from the bladder yielded organisms that were regarded as contaminants (diphtheroids) After dilatations of the urethra, a hysteromyomectomy was done One of several Wassermann reactions was positive, and she was given 16 doses of diarsenal and 15 of bismuth In 1935 she returned complaining of marked pain in the bladder and renal regions, with much dysuria and straining on urination The external genitalia were normal Two thickened folds were found on each side of the urethral meatus which was situated about 1 5 centimeters back of its normal position, and involved in a healed ulceration With great difficulty the urethra was again dilated The remainder of the pelvic and rectal examinations were negative Wassermann reactions were negative, Frei reaction positive The urinary symptoms and the urethral stricture have been temporarily helped by treatment

CASE 4 A P The patient, a negro female of 53 years, was first seen in 1920 at the age of 38, complaining for 20 years, of dysuria and of passing her urine in small amounts frequently and slowly One year previously she had a sore on one labium, which lasted only a few days For 2 weeks she had had constant dribbling Examination showed normal external genitalia There was a fold of vaginal mucosa, which had evidently been distorted by an inflammatory process, stretched across the urethral orifice in a bridge like formation After the band was cut the meatus was found extremely small A small probe indicated the lumen With some difficulty the urethra was dilated In 1935 she returned complaining of severe pain and great difficulty in emptying her bladder There has been marked frequency, nocturia, and slight incontinence Examination showed normal external genitalia The anterior part of the urethra was missing, being replaced by healed scar tissue The orifice was found with difficulty, being extremely small and situated about 2 centimeters back of its normal position With more difficulty it was dilated The remainder of the pelvic and rectal examinations were negative Repeated Wassermann reactions were negative, Frei test negative The ulcerative process was long ago completely arrested

CASE 5 M S The patient, a negro female of 32 years, was seen in 1929 complaining of vaginal bleeding following intercourse and nocturia A year previously, both she and her husband had had inguinal buboes which were incised and drained several weeks On examination there was found an inguinal scar, but the glands were not enlarged A small caruncle of the external urethral meatus was found The pelvic organs and rectum were normal The uterus was curetted, normal endometrium obtained, and the caruncle was fulgurated with high frequency current Following this, redness and induration persisted about the urethra, and there was some dysuria and nocturia In 1930, she contracted gonorrhea, proved by urethral smear In 1933, she returned with backache, dysuria, frequency, partial urinary incontinence, and some hematuria A reddened caruncle surrounded the meatus and three small punched out ulcerations were found on the lower part of the right labia Dark field examinations for spirochetes were negative on several occasions A diffuse stricture of the urethra and marked injection of the outer half of the urethra were present Eight cultures from the urethra on separate occasions were either sterile or gave varying organisms considered contaminants In 1934, the urethra was eroded to the internal sphincter which was the site of a stricture In 1935 she had practically no urinary complaints, was voiding easily, and while the urethra was found largely eroded away the ulceration appeared healed and not injected Biopsy of the ulceration showed chronic inflammatory tissue Several Wassermann reactions taken over several years were negative As for treatment, the urethral caruncle was originally fulgurated which apparently helped none Silver nitrate was occasionally applied to the ulceration, and the stricture was dilated as it became necessary A recent Frei test was negative The ulceration was almost completely healed

CASE 6 S J The patient, a negro female of 38 years, was first seen in 1932 complaining of headaches and pains in the lower abdomen At 19, she had had gonorrhea, followed a few years later by a genital sore causing a swelling on one side of the vulva, which afterward disappeared In 1926 she took needles for "bad blood" for 9 weeks, at another hospital It was not definitely known that this patient had had syphilis Examination showed normal external genitalia, and there was no urethral lesion A diagnosis of chronic salpingitis and retroposition of the uterus was made Although the Wassermann reaction was negative and continued so on 21 occasions, she was at that time given 8 doses of bismuth and 6 doses of neo-arsphenamine In 1933, she returned with more marked urinary symptoms and a diminution in the size of the urinary stream A small shallow ulcer with clean, freely bleeding base and measuring 2 centimeters across was found destroying the urethral meatus She was given 6 doses of neo-arsphenamine and 5 doses of bismogenal, while there was slow progression of the ulceration In 1935, the patient had a deep ulceration with a pinkish gray, firm, polypoid base which had destroyed about 2 centimeters of the urethra A biopsy of the ulcer showed chronic inflammatory tissue Frei reaction was strongly positive The ulceration was slowly progressing

CASE 7 R D The patient, a white widow of 35, was seen in 1935 complaining of ulceration about the urethra for 1 year, which began as an "abscess" in the urethra After a short time the abscess ruptured and did not heal For 4 to 5 years she had had burning and stinging on urination, with some dysuria These symptoms have been much more aggravated since the ulceration developed Several previous Wassermann reactions were negative, and a biopsy had shown chronic granulation tissue Three X-ray treatments had been given with no improvement On examination the external genitalia were found normal The anterior urethra was completely destroyed by a deep, reddened, undermining ulceration, with undulating thickened borders of the vaginal mucous membrane The base of the ulceration was quite red and polypoid, into which at some point the urethra opened The remainder of the pelvic and rectal examination was negative Repeated Wassermann tests gave negative reactions Biopsy again showed chronic granulation tissue Cultures for fungi were negative Frei reaction was positive The ulceration appeared to be slowly progressing

CASE 8 C J The patient, a negro female of 20 years,

Fig. Case 8. Undermining ulceration has destroyed the anterior part of the urethra. The orifice opens below the symphysis, which is clearly seen. A small fistula is present immediately below the clitoris.

was seen in 1933, complaining of pain in the right shoulder and leg, burning on urination and nocturia. The external genitalia and urethral meatus were normal. Cervical smear was positive for Gram negative intracellular diplococci. Wassermann reaction was positive. X ray showed a pyosalpinx of the left tube, attributed to syphilis. Eight injections of neoarsphenamine were given with marked improvement in the bone lesion. Treatment was continued in another clinic with 8 doses of diamesol and 6 of bismuth. After 7 months of treatment and with no apparent difficulty from the gonorrheal infection, a small punched out ulcer appeared below the clitoris, with surrounding hyperemia and tenderness. Gentian violet and mercurochrome were applied locally. Forty eight cubic centimeters of 1 per cent solution of tartar emetic were given intravenously in divided doses, and she was given 2 injections of neoarsphenamine and 4 of bismogenol, while the ulceration proceeded to destroy the anterior two fourths of the urethra. The base of the undermined ulcer was very red and extremely tender. In 1935 the inguinal glands were just palpable, the largest about 1 centimeter across, and the labia, perineum and clitoris appeared normal. The anterior urethra was completely destroyed by an undermined ulceration with thickened undulating borders, the base of which was made of grayish red, firm, polypoid tissue. The curving arch of the symphysis was readily seen. The pelvic organs and rectum were normal to palpation. Frei reaction was positive. The progression of the ulceration showed no evidence of being arrested.

Case 9. F. X. The patient, a negro female of 53 years, was first seen in 1930. Her menopause was in 1925 following hysterectomy, which she developed marked soreness in the region of the urethra. Since then she had had yellowish discharge, occasional spotting of blood, frequency and burning on urination, with occasional incontinence. There was nocturia once to three times. On examination, inguinal glands were not palpable and external genitalia were normal. The anterior urethral wall was greatly thickened, corrugated, indurated, and dry. The urethral meatus was normal. Two false orifices near the meatus did not communicate with the urethra. The remainder of the vagina, cervix, and rectum were normal. There were myomata uteri. Wassermann reaction was positive, and she was given 3 doses of neoarsphenamine and 3 of bismuth. In 1933 there was severe constant burning sensation in the region of the urethra and frequent bleeding from the urethra. A soft granular ulcerous lesion several centimeters across was located involving the urethral meatus. Six doses of bismuth, 40 cubic centimeters of tartar emetic (1 per cent) in divided doses, 2 doses of arsphenamine, and 3 doses of silver arsphenamine were given in succession. In 1933 the symptoms were not improved, and there was nocturia 4 to 5 times. Examination showed the urethra opening into large excavation with finger like processes, easily admitting the finger tip, bleeding easily and quite painful. A part of the overhanging mucosa was removed, and the bed of the ulcer fulgurated with unipolar current. Five doses of bismuth and 40 cubic centimeters of tartar emetic in divided doses were given. In 1935 the urinary symptoms had shown no improvement. The inguinal glands were not palpable. The labia majora and clitoris were slightly edematous. The deep, dirty red, granular ulceration extended under the clitoris and beneath the skin of the right labium majus forming a small perforation. The urethra opened into the ulceration far up beneath the symphysis. The cervix and rectum were negative. The myomata uteri had not increased in size. Several biopsies showed only chronic granulation tissue. Frei test was strongly positive. The ulceration showed no healing.

Case 10. C. A. The patient, a negro female of 25 years, was seen in 1934 complaining of irritated urinary sensation, dysuria, nocturia, chills, fever and pain in the right flank. Acute cystitis and pyelitis were evident. Examination showed the clitoris, right labia, meatus and urethra swollen, dotted with small pus areas. The anterior urethra was destroyed by an old ulceration extending behind the symphysis pubis and down the left side of the urethral orifice. The cervix and uterus were normal. Both adnexa were enlarged, fixed, and tender. Urine cultures showed Bacillus aerobacter aerogenes and Bacillus coli. The acute symptoms soon subsided. In 1935 she had slight burning on urination and slight incontinence, but no pain, dysuria, or hematuria. A chain of inguinal glands was just palpable in each inguinal region. The right labium majus was three times normal size, the left slightly swollen. The clitoris was large, measuring 3 by 5 centimeters. The urethral meatus was completely destroyed by deep ulceration with firm, red polypoid base. The arch of the symphysis pubis was clearly seen, and the cavity admitted one finger tip to the internal sphincter of the bladder. Rectal examination was normal. Biopsy from the ulceration showed chronic granulation tissue. Culture from the bladder yielded only Bacillus aerogenes. Repeated Wassermann reactions have been negative. Frei test was positive. There was no evidence that the ulceration was healing.

Case 11. L. J. The patient, a negro female of 23 years, was first seen in 1927 with vascular rash over the back and pouch (Wassermann reaction). The labia were slightly swollen, and there were small ulcerations on the clitoris and both labia majora. She was given 9 injections of neoarsphenamine and 5 of bismuth, and the ulcerations healed. In 1929, small, very hard granular oval ulceration was found on the inner surface of the left labium majus. Several inguinal glands, 1 to 2 centimeters in diameter, were palpable on each side. Dark field examination and Wasser

mann reaction were negative In 1930, the labia appeared normal In 1931, a small lesion on the vulva was dark field positive for Treponema pallidum The vulva was swollen and edematous Wassermann reaction became positive, and the labia became more edematous A large ulcer appeared on the left labium majus with ragged edges and dirty gray base Five doses of arsphenamine and 55 cubic centimeters of tartar emetic were given in divided doses as the lesions progressed Malaria inoculata was given, resulting in 12 chills The labia were enormously swollen with hard, raw, indurated areas between the labia, and a boil like localized lesion appeared on the left buttock Ten doses of neoarsphenamine and 155 cubic centimeters of tartar emetic in divided doses were given, with practically no change In 1935, the patient complained of frequency and burning on urination and nocturia, 2 times There was a constant dull aching pain in the vaginal region On examination the inguinal glands were found palpable but not definitely enlarged Both labia majora were very large with induration in the skin A deep ulceration had destroyed the urethral meatus, extended around the introitus and formed deep pockets on each side of the rectum, more on the right side The vagina behind the ulceration and the cervix appeared normal Rectal examination was negative Frei test was positive There was no evidence that the ulceration was healing

From the histories and physical findings of these individual cases, certain characteristics of the urethral lesions group themselves to form a syndrome The disease apparently begins as a chronic urethritis, which may be accompanied by an intra-urethral ulcer, and may remain stationary for years, with or without treatment Apparently, if the inflammatory reaction extends deeply into the tissues, the disease may proceed so slowly as to allow progressive formation of scar tissue, resulting in stricture of the lumen The stricture may occur at any point, but is most commonly near the internal sphincter In some cases the inflammation extends at a steady rate, involving most severely the urethral meatus, resulting in ulceration of the orifice The ulceration may proceed, causing all degrees of destruction of the urethra and surrounding vaginal mucous membrane, although we have not seen complete destruction of the internal urethral sphincter or base of the bladder These ulcerations have a firm, granular, polypoid base, 0 5 to 2 centimeters deep, with characteristic thickened, undulating, undermined borders The base may be very red, extremely tender, and may bleed easily, or it may be gray granular, and insensitive The ulceration may be entirely replaced by the contraction of scar tissue and a lesion may be partially or entirely halted in such a manner at any point The ulceration may extend around the introitus and burrow deeply to each side of the rectum There may or may not be an associated elephantiasis of the vulva

Six of the 11 cases presented in this paper have had syphilis and have been treated with arsenic and bismuth preparations These cases follow

Fig 2 Case 10 Elephantiasis of the labia majora and clitoris accompany a deep ulceration destroying the urethra up to the sphincter

One of the 2 patients with chronic urethritis had syphilis Her urinary symptoms began shortly after a rather thorough course of antisyphilitic treatment

One of the 2 patients with urethral stricture had syphilis Symptoms from the stricture began several years after antisyphilitic treatment, and the stricture was not helped by repeated antisyphilitic therapy

Four of the 7 patients with definite ulceration about the urethra had syphilis, and in each of these cases the ulceration appeared during the time the patients were under observation and receiving antisyphilitic treatment Furthermore, a continuation of vigorous antisyphilitic treatment not only had no effect on healing the lesion but was accompanied by a progression of the ulceration in each case The 3 other cases with ulceration, having almost precisely the same characteristics, had repeatedly negative serological tests for syphilis In fact one of the latter with a typical ulceration of 2 years' duration showed in 1935 the greatest degree of healing of any of the patients with ulceration and had received only hygienic local treatment in addition to local applications of silver nitrate

Biopsies were taken from 5 of the 7 patients with ulceration In each case sections showed for the most part a chronic granulation tissue with rather marked proliferation of the endothelium of the capillaries and a marked infiltration with plasma cells and lymphocytes In addition there

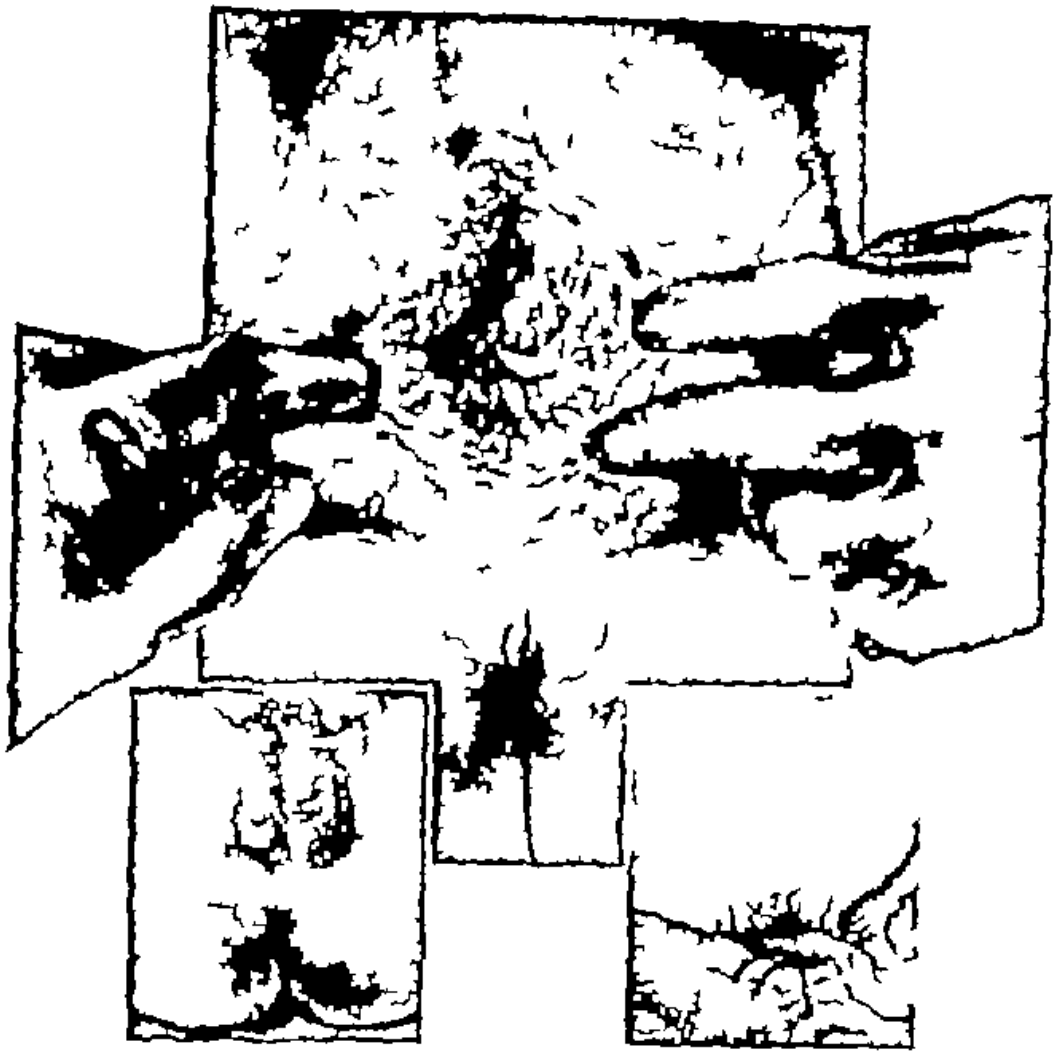

Fig. 3. Case [illegible]. External genitalia of a 21 year old negress showing elephantiasis vulvae and complete ulceration of the vestibule. The urethra opens in the depth of the ulceration and hypertrophic tags surround the vaginal orifice. To the right of the vaginal orifice the ulceration extends more deeply in the region of Bartholin's gland. The skin over the buttocks shows induration with superficial infection (left insert). Sagittal section shows extent of the ulceration, which destroys the anterior urethra and vagina (right insert). A probe designates the depth of the ulceration in the region of Bartholin's gland.

were scattered polymorphonuclear leucocytes, and occasional eosinophils and mast cells. The surface epithelium where present showed some hyperkeratosis with scattered polymorphonuclear and round cells through the squamous cell layer. The rete pegs at the edges of the ulcer were greatly prolonged, and the basal cell layer in some areas, became two and three layers thick. However the basal layer was intact and no mitotic figures were seen. In some cases there was great scarring in the submucosa. No obliterative changes were seen in the small vessels.

Histologically no formation of tubercles was found. Kinyoun stains of the cases with biopsies were negative for tubercle bacilli. Other bacterial stains revealed no bacteria within the tissue itself although Gram positive and Gram negative cocci and bacilli were present in relatively small numbers in the surface débris. No organisms with the morphology of Ducrey's streptobacillus were found. No Gram negative diplococci, either intracellular or extracellular could be demonstrated. Wright's stains showed no Donovan bodies.

Frei tests were performed on the 11 patients, with positive results in 9. One patient (Case 4) with a negative test was a negro woman with scarred retracted urethral meatus and urethral stricture, first discovered in 1930, and at that time the history of the lesion dated back 30 years. No active ulceration has been observed. The other patient (Case 5) with a negative test was a negro woman with an ulceration quite similar to the

others in this group, which destroyed the anterior portion of the urethra, but which was gray, scarred, and insensitive In both of these cases the Wassermann reaction was negative

The Frei test is based on the development of allergy or hypersensitivity to the virus This phenomenon has been thoroughly studied in numerous bacterial infections, particularly tuberculosis Obviously, in the preparation of the antigen, as stated by Frei himself, it is of the utmost importance to use material from a definite case of lymphopathia venereum, in which other venereal diseases have been excluded to make certain of bacteriological sterility, and to avoid overheating Two reasons have been advanced in the literature to explain negative reactions in rare cases where there is every indication from the clinical picture to expect a positive test The first is quite valid, that of anergy, or lack of allergy That allergy varies, and even disappears in all infections is well known The second is that there may be two types of the virus of this disease with extremely slight clinical differences, but acting as separate antigens with individual allergy (Hermans, Coutts)

TREATMENT

In the treatment of lymphopathia venereum, numerous drugs have been used, including arsenic, antimony, manganese, and gold compounds Antisyphilitic treatment has been shown to have no effect Tartar emetic is most widely used, and while many observers have claimed good results, others have not met the same success This drug acts as a specific in the treatment of granuloma inguinale, which probably explains the attempt to extend the use of tartar emetic to lymphopathia venereum The confusion of these two diseases has been discussed The great number of drugs that have been brought forth speaks for the unsatisfactory status of treatment

Various authors have advocated daily intradermal injections of Frei antigen, or the intravenous injections of large doses of antigen Still others have used the antigen as local applications

Kalz and Sagher have used drugs, radiation, and immune serum, obtaining best results from the latter

In the cases reported in this paper antisyphilitic therapy and tartar emetic had no apparent effect High frequency fulguration (2 cases), X-ray (1 case), and malaria inoculata (given for another reason, 1 case) had no beneficial effects Two patients with the least treatment showed the greatest healing

It would seem that cure of lymphopathia venereum probably results only when the individual becomes immune to the virus In no known virus disease is there a specific drug therapy The transfer of passive immunity by injection of serum from individuals with healed lesions seems to offer the greatest possibilities in the treatment of this disease, although few studies of this method have been made

SUMMARY

1 Eleven cases of disease of the urethra occurring in women are presented The disease presents a syndrome—a chronic urethritis, with or without intra-urethral ulceration, which may remain extremely chronic and indolent or may proceed to urethral stricture, or to ulcerative destruction of the urethra, the ulceration may extend beneath the clitoris and labia, or about the introitus and deeply to the sides of the rectum, elephantiasis vulvæ may be associated

2 The presence of positive Frei reactions in 9 of the 11 cases indicates that this syndrome is probably due to the virus of lymphopathia venereum—"lymphogranuloma inguinale"

3 A wide variety of parenteral and local treatment had no appreciable influence on the disease Two patients with least treatment showed the greatest healing The indications are that cure, as in other virus diseases, probably depends on immunity

For helpful criticism, we are indebted to Drs Thomas S Cullen, Arnold R Rich and J Earle Moore For the drawings, we thank Mr Jack B Wilson

NOTE —Since this paper has been submitted for publication, 14 additional cases of this syndrome have been studied (13 negro women and 1 white) In 6 the Wassermann test was positive, and in all 14 the Frei test was positive

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PLASTIC OPERATIONS FOR CONSTRUCTION OF AN ARTIFICIAL VAGINA

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ALTHOUGH fully five hundred cases of operation for construction of an artificial vagina have been reported in surgical literature of the world no generally accepted method has as yet been described The many techniques used fall into two main groups namely (1) those in which the lumen of the artificial vagina is lined with skin and mucous membrane introduced as free or pedicle grafts and (2) those in which the vaginal canal is formed by a transplanted segment of the intestinal tract Operations making use of skin and mucous membrane grafts are undeniably safer than intestinal transplantation, and apparently the end-results can be equally as good Consequently, we believe that this second group of dangerous methods should be condemned and efforts directed toward improvement of the safer technique

During the complicated embryonic development of the genital tract, the mullerian ducts may fail to fuse normally throughout all or portions of their lengths The results of faulty or incomplete fusion are many and varied and may involve fallopian tubes, uterus or vagina alone, or any of these organs in combination Usually when there is complete absence of the vagina, the external genitalia are normal, as are the ovaries and secondary sexual characteristics The uterus may be absent or rudimentary, but occasionally is normal

When the uterus is absent or physiologically inactive and there is no vaginal canal, these abnormalities often remain undiscovered until the patient marries or is examined to find the cause of amenorrhea The discovery not infrequently produces a profound mental shock To all appearances, she is a normal, healthy young woman She has an abundance of the female sex hormone She may have married or contemplated marriage with the expectation of assuming her full share of conjugal and family responsibilities In such a case the construction of an artificial vagina should undoubtedly be attempted But to what extent is the surgeon justified in hazarding his patient's life in order to provide for her an organ of coitus? In extreme cases when severe depressive psychoses are present, and even suicide threatened, extreme measures for relief, if they were necessary, might be considered But when equally as good results can be obtained with the use of less dangerous procedures, unnecessary risks should not be taken

We believe that the objections to the earlier skin grafting methods have been largely overcome In the first place, such operations as those described by Frank and Geist, Graves, and Davis and Cron, are approaching closely the solution of the technical problem Secondly, while the operative technique is of great importance, it has been learned that the postoperative management of the cases is of practically equal importance The chief cause of failure in early operations of this type was scar formation and contracture which rapidly closed the lumen of the artificial vaginal canal Dilatation is the solution to this difficulty Dilatation should be begun early repeated frequently, and prolonged indefinitely Our first case, the report of which follows, illustrates strikingly the importance of dilatation in obtaining a good result This operation was done by one of us Dr C W Lynn—in 1915 following the earliest and simplest technique of lining an excavation between the bladder and rectum with free grafts of skin and mucous membrane cut from the external genitalia Dilatation was begun early by mechanical means, the patient married, and dilatation has been continued by natural means for a period of 19 years, during which time the artificial vagina has functioned perfectly as an organ of coitus

Heppner, in 1872, first used skin from the labia and thighs to line an artificial vaginal canal Scarring and contracture impaired the success of his attempts To avoid this difficulty Baldwin, in 1904, suggested the formation of an artificial vagina from a double loop of small intestine or sigmoid brought down with its blood supply into an opening made between the bladder and rectum He performed the first operation by this method in 1907, and the same operation was done independently by Mori of Japan about the same time Schubert in 1911 modified Baldwin's method by detaching the rectum, moving it forward to be used as a vaginal canal, and bringing the sigmoid down to the anal orifice These methods soon became popular, especially in Europe, and are at present preferred by many operators in spite of the operative mortality (variously estimated at

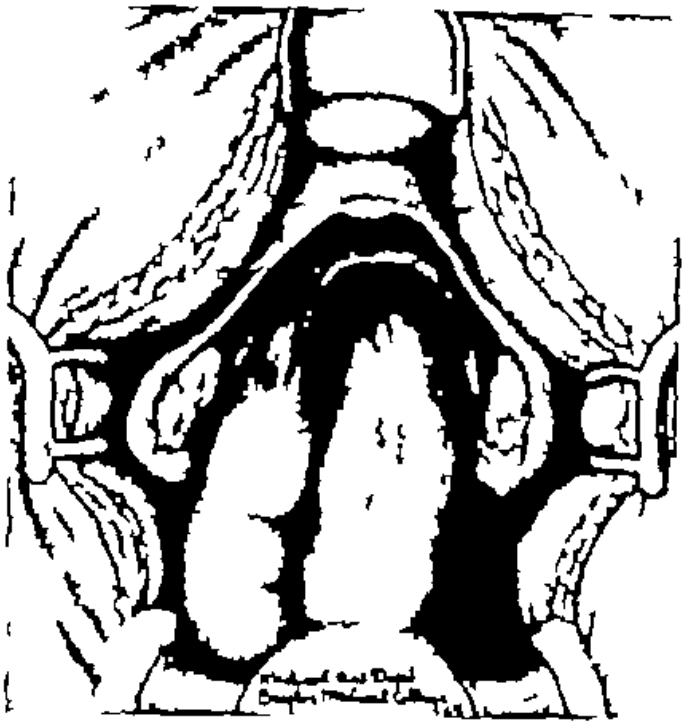

Fig 1. Case View of the pelvic organs showing the rudimentary uterus and tubes, normal ovaries, and pelvic kidney

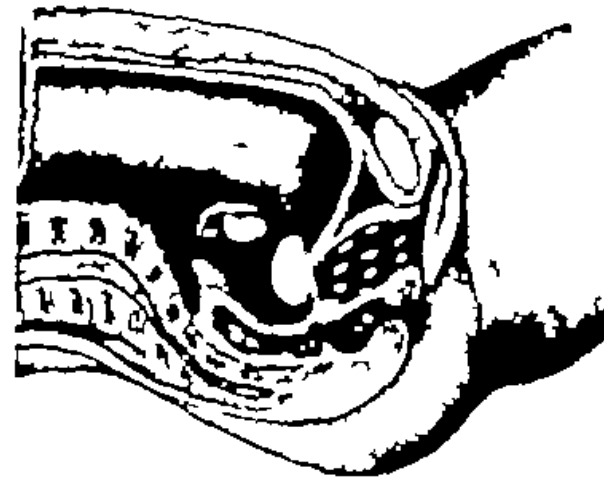

Fig 2 Case 1 A schematic drawing of the pelvis and artificial vagina in sagittal section showing free grafts in place

6 to 17 per cent) and not infrequent occurrence of serious complications such as cellulitis, peritonitis, incontinence, fistula etc.

Returning to the safer skin grafting principle Graves, in his textbook (1916) described an operation in which four pedicle flaps were used two from the minor labia and two from the thighs, and sutured together and inverted into the space prepared between the bladder and rectum It is difficult to obtain a vagina of sufficient depth by this method. What seems to us to be the best method so far described is that proposed by Frank and Geist in 1927 They used a single tubed pedicle flap from one thigh with delayed transfer which allowed them to obtain sufficient depth, and adequate blood supply to the graft was supplied while it was becoming established in its new location They emphasized the necessity for early and adequate dilatation of the tube. The originators of this method have reported 4 cases and 1 each has been reported by Rushmore, Turrenne, and Grad Our second case was done by this method, which makes 8 cases reported with uniformly good results and no deaths.

Case Patient, unmarried, aged 20 years, was admitted to the hospital August 3 9 5 The vagina was absent and she complained of cramping pains in the abdomen The patient had been in excellent health and had developed normally during infancy and childhood At 5 years of age she began to complain of frequent attacks of cramping pain on both sides of the lower abdomen She began to have frequent headaches and complained of being easily When at 6 years she had not menstruated, she was examined by the family physician who discovered the absence of a vagina The abdominal pains gradually became less severe, but she continued to have headaches and was constantly nervous and irritable About a month before the date of admission, the abdominal cramping returned, together with nausea, both of which persisted

Physical examination revealed well developed and well nourished young woman The breasts were large and well forward, and there was normal female distribution of hair over the body The external genitalia were normal There was a hymen with small slit like opening, but instead of vagina there was only blind pouch about centimeter deep By rectal examination, small, tender mass could be felt in the location of the uterus

Operation Under general anesthesia, low right rectus incision was made and the pelvic and abdominal cavities explored (Fig) There was *small rudimentary uterus* situated low in the pelvis The fallopian tubes were present, but were contracted to mere fibrous cords in their proximal three fourths Both ovaries were normal in appearance, but the left was densely adherent to the posterior *surface of the broad ligament* The right kidney was normal in size and location, but the left kidney was situated in the brim of the pelvis Its ureter was proportionately short and its blood supply came from an artery leaving the aorta at its bifurcation The appendix was irregularly *thickened due to the presence of fecoliths* in the lumen

Since gestation was obviously impossible and there was a possibility of retention of menstrual products the endometrium bearing portion of the uterus was removed, together with the left tube and adhered ovary The appendix was also removed, and the incision closed

The patient was then placed in the perineal position and transverse incision made through the stratified mucous membrane of the vaginal pouch Through this incision the bladder and rectum were separated by careful blunt dissection until the peritoneum of the cul de sac was reached and the cervical stump of the uterus felt The cavity thus formed was 10 to 1 centimeters in depth, and easily admitted three fingers After all bleeding was controlled, the cavity was lined with free full thickness grafts of skin and mucous membrane obtained from the vulva (Fig 2) The labia minora were completely excised and formed the

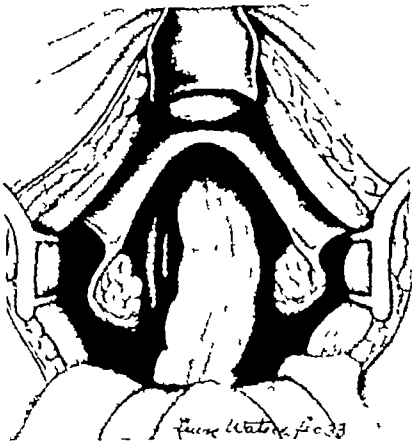

Fig 3 Case 2 View of the pelvic organs showing absence of uterus, rudimentary tubes, and normal ovaries

greater part of the grafted skin The grafts were sutured loosely in place with fine plain catgut A plug of rolled gauze, covered with rubber tissue and lubricated with vaseline, was inserted into the cavity to exert a constant uniform pressure upon the grafts

The original plug was removed after 1 week The grafts were inspected and all were found to be taking The plug was replaced by a device designed to act as a constant dilator This dilator was constructed of a large rubber bougie 10 centimeters long, mounted with a hinge joint on a curved piece of metal which fitted against the symphysis pubis and the perineum, and was held in place by straps and a belt This device was worn constantly night and day for 6 months except when it was removed once a day so that a cleansing douche could be taken While healing was taking place, it was necessary to use silver nitrate to cauterize the granulations growing up between the grafts Healing was complete with a minimum of scar tissue after about 6 weeks

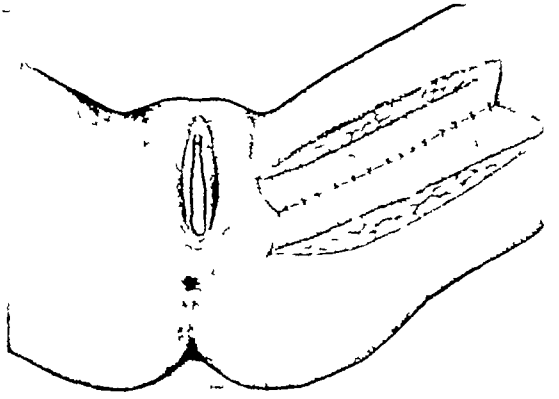

Fig 4 Case 2 The tubed skin flap on the left thigh

This patient was married 1 year after the operation A communication from her husband dated August 24, 1934, states that the sexual relationship has been normal and entirely satisfactory to both husband and wife ever since their marriage. The vagina is 4½ inches deep There is still a tendency for the lumen to contract when sexual intercourse is omitted for longer than 2 or 3 weeks, but there has never been any difficulty in dilating it.

Case 2 The patient was married, aged 18 years She was admitted to the hospital April 24, 1933 Her complaints were absence of menstruation, abnormality of genital organs, lower abdominal pain The patient had been an apparently normal girl, and although she never menstruated, the breasts and other secondary sexual characteristics had developed normally At intervals of 3 to 4 months during the past 3 years, she had dull pains in both lower quadrants, especially the right, and some backache Otherwise there were no physical complaints Six months ago she was married, and for the first time discovered that she had no vaginal orifice and normal sexual relations were impossible On consulting a physician in the small community where she lived, she was told that there

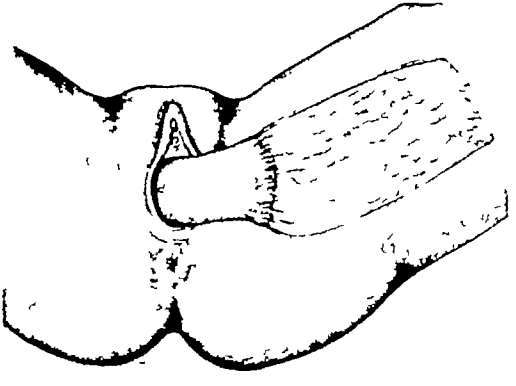

Fig 5 Case 2 The distal pedicle of the flap has been severed and the free end transplanted into the space made in the loose tissue between rectum and bladder

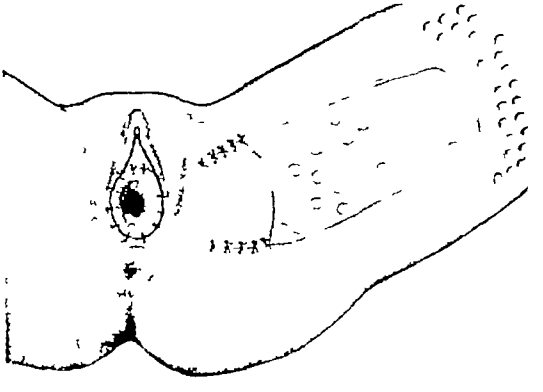

Fig 6 Case 2 The proximal pedicle has been severed and returned to its original site Small deep skin grafts are applied to the defect on the thigh. The tube graft is sutured in place

was an absence of the vagina and uterus about which nothing could be done and she and her husband were advised to have their marriage annulled. Not to be discouraged they sought other advice.

The patient was a robust, attractive young woman. No abnormalities were discovered except those of the pelvic region. The external genitalia were absolutely normal in appearance save for the sole fact that a pliable membranous diaphragm completely closed the region where the vaginal orifice should have been. This had the appearance of a imperforate hymen. Rectal examination, however, revealed no evidence of the presence of uterus or a vagina. A small mass high in the right side of the pelvis was thought to be an ovary.

The patient was anxious to submit to any surgical procedure which might offer a chance for correction of any part of her abnormality.

Operations. The first stage was done April 25, 1911. The first procedure was an exploratory laparotomy under general anesthesia for the double purpose of discovering if possible the cause of her recurrent pain and to determine whether any remnant is of the uterus or vagina remained which might be used in the plastic restoration contemplated. This operation showed that the vagina was absent entirely and that the uterus was represented by only a thickened ridge extending upward on each side of the pelvis from the depth of the pelvic floor and each ridge widening out at the brim of the pelvis into a much shortened fallopian tube with a normal fimbriated end. Both ovaries were located in their usual positions, and were normal in size and appearance (Fig. 3). The appendix was elongated, bound to the cecum with old adhesions, and contained several fecaliths. It was removed and the incision was closed. The patient was then placed in the perineal position and the first stage of an external plastic operation for artificial vagina was done. This consisted of partially raising a tubed skin flap from the inner side of the left thigh with proximal attachment at the edge of the labium major. This tube was about 8 inches long and 1½ inches in circumference (Fig. 4, method of Frank and Gerst).

The second stage was done May 1, 1911, 6 days after first stage. The flap was completely undermined. Local anesthesia with novocain was used.

The third stage was done May 5, 1911, 10 days after the first stage and consisted in cutting across the distal pedicle after testing with clamp (blanching of one third).

The fourth stage was done May 7, 1911, 7 days after first stage. The pedicle was severed and closed. The free end was transplanted into the bed made by the loose tissue between the bladder and the rectum through a transverse curved incision in the hymenal diaphragm. The lumen of the tube was filled by a plug of iodine gauze. A retention catheter was placed in the bladder (Fig. 5).

On May 1[illegible], 1911, the fifth stage was done, 27 days after the first stage. The cutting across of the proximal pedicle of tube began. The iodine gauze plug was removed and the lumen of the tube was irrigated daily because of purulent material from the depths. A hard rubber dilator replaced the gauze pack.

On May 3[illegible], 1911, the sixth stage was done, 30 days after the first stage. The pedicle was severed and the tube replaced in the original bed on the thigh. The remainder of the bed was grafted with small deep graft (Fig. 6).

Patient was discharged June 2[illegible], 1911, 47 days after the first stage. No evidence of infection remained. The vaginal canal was 3 inches deep, and admitted two fingers.

A follow up, 6 months after operation, improved. A vagina functioning satisfactorily to patient and husband. The dilator had been kept constantly in place for 2[illegible] months, then coitus began, and the dilator was inserted twice daily.

A follow up, 18 months after operation, revealed that there had been some contracture of the inner end of the tube but the mucocutaneous junction had been drawn forward about 2 centimeters. The vagina still admitted two fingers to a depth of 3 inches. The uterine rudiment could be felt as a slight ridge. The skin of the tube is soft, pliable and moist.

Although we are presenting Case 1 as an example of the excellent results which can be obtained by a simple operative method, we do not believe that the use of free grafts to line the cavity of the artificial vagina will be uniformly successful.

The employment of pedicle flaps as described by Graves or preferably the tubed pedicle flap of Frank and Gerst will be much more likely to ensure healing with a minimum of scar tissue and hence eliminate to a large extent the undesirable effects of contracture. Also we wish to emphasize the great importance of adequate dilatation of the artificial lumen which must be begun early and continued indefinitely.

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THE OCCURRENCE OF DIFFERENT TYPES OF BRAIN TUMORS IN ONE PATIENT[1]

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WE are all familiar with the occurrence of different types of tumors in one and the same patient Countless patients may have some form of benign tumor on the external surface of their body, fibromas, lipomas, and the like, and then develop a malignant tumor in some other portion of the body Nobody, I believe, has ever taken particular notice of this fact or attached any importance to it Then again, we have all seen cases in which a benign tumor, either due to trauma or some other irritation, has undergone malignant degeneration

There are instances, however, in which multiple tumors occur in a patient, in these instances the evidence seems overwhelming that some fundamental condition exists in the organism which predisposes to tumor formation I lack the special training to discuss the basic principles involved but would like to draw attention to several such cases that I have encountered in my service in the course of the past 15 years

There are 4 such cases, of which I want to speak particularly

The first one was a man who had an acoustic nerve tumor, of the von Recklinghausen type, which was removed by the intracapsular method 8 years ago Until a month before admission he had carried on his work as a railroad engineer without difficulty, when he developed symptoms of recurrence At a second operation, there were found bilateral eighth nerve tumors, a recurrence at the original site having become enormous He died after an attempted removal Autopsy revealed five other tumors besides the two in the region of the eighth nerve One of these was an osteoma and at least two others were meningiomas (Figs 1 and 2)

The second case was a patient with an acoustic neuroma who died suddenly and had an unsuspected, enormous right frontal meningioma which had given no symptoms whatever

The third case which perhaps should not properly belong in this group and yet has points of similarity, is that of a woman on whom I removed, I thought completely, a meningioma compressing the cord Fifteen years later she developed a recurrence at the same site She had been free of symptoms for 14½ years

The fourth case is one which I wish to report in greater detail A boy of 17 years who all his life had the picture of a von Recklinghausen's disease with countless small tumors some elevated and others merely the well known

Fig 1 1, Osteoma, 2 and 5, meningiomas, 3, 4, and 6, perineurial fibroblastomas

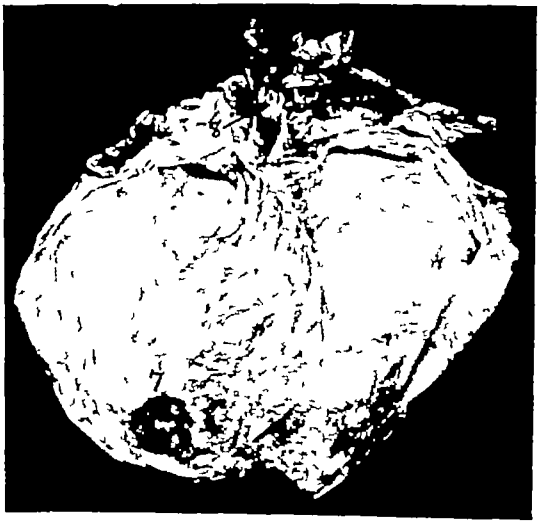

Fig 2 This was the dura with two of the tumors attached, 7 and 8, correspond to 2 and 5 seen in Figure 1—both meningiomas

[1]Presented at the fifth congress of the Pan American Medical Association March 1934

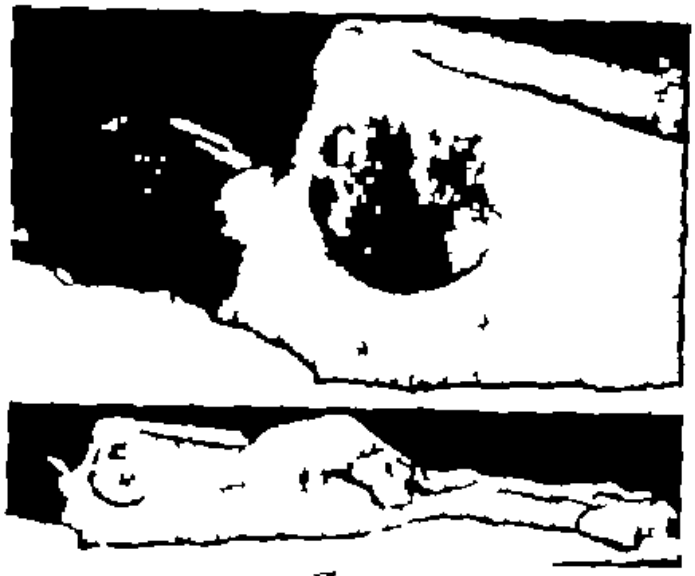

Fig. 3

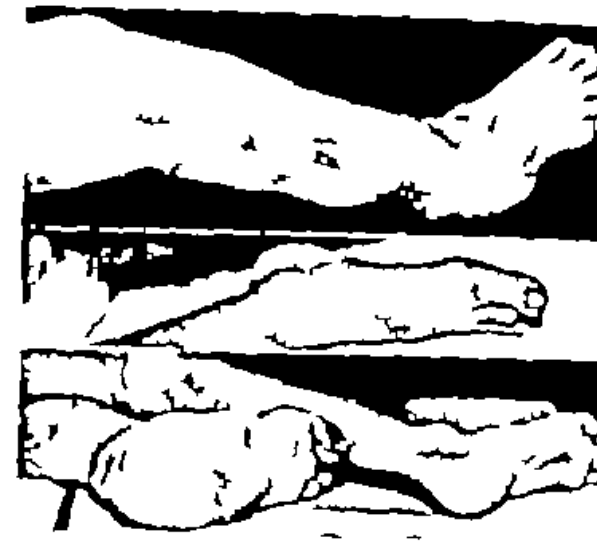

Fig. 4

Fig. 5

Fig. 6.

Figs. 3 and 4. Typical picture of von Recklinghausen's disease. The enlargement of the foot and the areas on the back are less usual in this disease.

Figs. 5 and 6. The collection of air at *A* (Fig. 5) in the view has the location but not the shape of the third ventricle. It is only in the lateral view (Fig. 6) that it is evident that the collection of air is displaced lateral to the ventricle, which had been pushed over by the large cyst which occupied the entire right frontal lobe.

café au lait spots on his body. In addition, he had two large tumors, elephantiasis nervorum, one on his back and one on his foot (Figs. 3 and 4), also changes in one tibia as has been described in von Recklinghausen's disease. This patient developed the symptoms of a brain tumor and, when admitted to the hospital, had a high grade of choked disc in both of his eyes, with a history of recent loss of vision and, still more recently, a bilateral loss of hearing.

Examination suggested that we were dealing with a right frontal lobe lesion. An unusual series of air plates confirmed this idea (Figs. 5 and 6). At operation I removed a large glioma-form cyst of the right frontal lobe, a typical astrocytoma, the cystic portion containing over one cubic centimeter of fluid and the solid portion extending over the gyrus. The boy's hearing has improved markedly and all but the highest tones have completely returned. Evidently this loss of hearing was a pressure phenomenon and was not due to an actual destruction of the auditory mechanism.

The occurrence of different types of tumors in a patient with von Recklinghausen's disease has been reported before, but, in all instances that I am familiar with, the tumors have all belonged to the fibroblastic group Here, however, is an instance of a tumor with an entirely different embryological origin The accepted idea today in regard to astrocytomas is that they are a form of glioma and develop from the brain tissue itself This case therefore raises two interesting points

1 Does some condition exist in von Recklinghausen's disease which stimulates the growth of certain tissues in the body?

2 Does the particular type of glioma known as an astrocytoma belong to a different category and should we perhaps not include it in the glioma group, or does the unknown stimulating factor observed in von Recklinghausen's disease also affect other tissues than those of connective tissue origin?

UNDULANT (MALTA) FEVER OSTEOMYELITIS AND ARTHRITIS

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THE incidence of arthropathies and hydrarthroses complicating undulant fever is being and has been noted in the more recent medical literature Bone lesions also have been observed but stressed very little In the Ohio series of 175 cases of malta fever, Simpson finds 31 per cent arthropathies In the Iowa series of 375 cases, Hardy quotes 32 per cent arthropathies, 1 case of hydrarthrosis and 1 of osteomyelitis Baker reported an interesting case of intermittent hydrarthrosis Weil has reported a case of hydrarthrosis of the foot due to malta fever and pointed out that this may occur either during the febrile period or long after its resolution Zdrodowski reports 17 5 per cent bone or joint lesions occurring experimentally in guinea pigs inoculated with Brucella abortus O'Donoghue recently reported a septic hip case due to Brucella melitensis, with pus formation which went on to bony ankylosis Kulowski and Vinke were apparently the first to report an actual pus lesion occurring in the spine from which focus the brucella was recovered in culture

Undulant fever is a general infection caused by one of the subspecies of Brucella melitensis The natural habitat of these organisms is in the domestic animals, in which there is a widespread distribution For man, the principal contact sources are cattle, goats, sheep, and swine Undulant fever in man and infectious abortion in animals remained unrelated until Evans indicated in 1918 the close relationship existing between the organisms causing the two diseases Although epidemics of infectious abortion in domestic animals have existed since the dawn of history, the causative organism was not discovered until 1895 by Bang and von Stribolt In 1910 MacNeal and Ken isolated the specific organism from cattle in the United States The first human case originating in the United States was reported in 1905 by Craig In Iowa the disease is as prevalent as typhoid and paratyphoid according to Hardy who collected 1,430 cases in continental United States prior to 1929 The following classification of this organism has been suggested by Hardy, Jordon, Borts, and Hardy

1 Brucella melitensis, variety melitensis

2 Brucella melitensis, variety abortus (bovine)

3 Brucella melitensis, variety suis (porcine)

The most severe infections result from the melitensis variety In Iowa it is believed that the abortus and suis varieties are equally responsible for the morbidity of undulant fever in man

Human infection results from contact with infected animals through ingestion of raw dairy products or from handling live stock as fresh meat The incubation period varies from 10 days to 3 weeks The irregular multiform symptoms of the disease are well known, but it should be remembered that *cases presenting abscess formation may be expected to show a chronic continuous low grade temperature without periods of remission* Of the greatest clinical importance have been the more recent reports of cases running a short course of a week or two In these patients the condition might very easily be mistaken for influenza or a respiratory infection The diagnosis is established by the agglutinin test, by skin tests, by blood culture, and by isolating the organisms from abscesses, from the urine, and sometimes from the stools

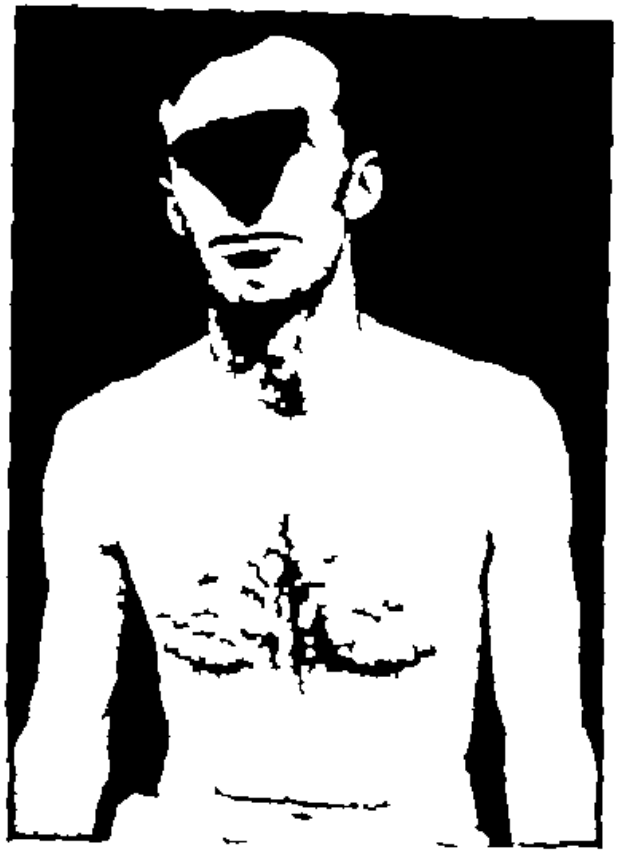

Fig. 1. Patient completely healed when last seen in April, 1934, and in good general health. No local or general subjective or objective symptoms. (Case 1.)

Fig. 2. Roentgenogram of humerus in 1934, showing the healed state of the lesion. There is nothing to distinguish this from an ordinary pyogenic osteomyelitis, except the tendency to localization and rather mild general cortical, and absence of periosteal, reaction. The joint is not involved. (Case 2.)

Perhaps malta fever involvement of the bones and joints is uncommon but there is a certain satisfaction in making the diagnosis as in all unusual conditions. However I feel strongly that in certain sections of the country many such specific infections are being overlooked chiefly because the possibility of malta fever is not thought of. There is another most important practical reason for making an accurate bacteriological diagnosis in this and other uncommon infections of bones and joints. Here especially secondary infection must be sedulously avoided. Malta fever is a self limited disease in most instances and proper drainage of localized abscesses will lead to cure. Secondary infection is a surgical disaster prolongs the course of the disease and may threaten the integrity of the part affected or even the life of the patient.

The clinical material in this series comprises osseous and joint lesions in 5 adult males: 2 instances of spondylitis, 1 of a humerus, 1 wrist joint and 1 instance involving the skull and ribs. Of these all but the humerus infection were diagnosed early as due to the brucella organism. The latter case was observed for almost 6 years before the real causative organism was suspected and recovered from the lesion. Three of the patients were employed about stock, one was a machanist, and the last a missionary who was infected in Africa. In only 3 of these cases did the systemic reaction lead to the suspicion of malta fever. Four were complicated by local suppurations which necessitated surgical drainage. One case of spondylitis did not suppurate and was finally healed by a bone graft fusion. Two of these were complicated by other lesions which led to some confusion in the differential diagnosis.

Because this series is relatively large there are several worthwhile points that warrant emphasis. Here, as in most acute infectious diseases, the osseous system is attacked rather late in the course of the disease. In 2 instances, however these manifestations came on at the onset of trouble (Cases 1 and 3). In two instances local symptoms came on suddenly and in 2 cases rather insidiously. These manifestations were usually of a low grade nature and did not necessarily give rise to a constitutional reaction. Final suppuration occurred twice, a seropurulent reaction in one and a non-suppurative lesion of the spine in which the bodies of the vertebrae were apparently attacked early (Case 2). The spondylitis lesion (Case 3) finally showed vertebral body invasion probably due to secondary invasion with the Staphylococcus aureus at a much later date. These suppurative lesions are amenable to surgical drainage and rest, the greatest care being exercised to prevent secondary infection. (Our method) The pathological inflammatory re-

actions are variable Of the multiform bacterial causative organisms in pyogenic osteomyelitis and arthritis the Brucella melitensis must be given serious consideration

CASE REPORTS

CASE 1 John S (D7170), aged 37 years a white American farmer was first admitted to the hospital in August, 1928 A diagnosis of malta fever osteomyelitis of left humerus was made The history indicated an insidious local onset with limitation of abduction of the left arm at the shoulder, of 4 years' duration and accompanied by moderate pain of limited duration There was no definite constitutional reaction One year before his admission an abscess was incised over the left deltoid region which continued to drain until 4 months ago Upon examination there was noted a small deltoid sinus and some induration and crepitation about the left shoulder joint with restriction of abduction due to muscle contracture The X-ray picture revealed a quiescent cavity in the upper left humerus No treatment was advised

In April, 1932, he still complained of some pain about the affected shoulder The pain radiated to the elbow There had been no fever or other general reaction There was 45 degrees of active and 70 degrees of passive abduction at the shoulder In June, 1932 the lesion was operated upon and the brucella organism was recovered The blood agglutination was also strongly positive Recovery followed

CASE 2 Lester K (F1486), aged 22 years, a machinist was admitted to the hospital in March, 1931 Diagnosis malta fever spondylitis

Patient's present illness dates back 6½ months at which time a diagnosis of malta fever was made by his attending physicians His last fever episode had ended 1 month ago About 2 weeks ago there first developed an insidious low back pain unaccompanied by any constitutional reaction or other general symptoms referable to his 6 months' old systemic infection One week ago this symptom became very severe and forced the patient to bed The pain was sharp, intermittent, radiated around the lower abdomen and was aggravated or provoked by any movements involving the spine The patient looked ill and was in obvious pain, thus making the examination difficult.

On examination the abdomen was found somewhat tense and rigid There was definite psoas muscle spasm There was a slight low dorsal kyphosis, marked localized tenderness limited to the dorsolumbar region There was pain on percussion and the spine was held rigid There was definite muscle spasm. The root pains were aggravated on coughing The liver was slightly ptosed but not enlarged The spleen was not palpable.

Laboratory examination revealed tuberculin tests, negative, urine, negative, hemoglobin, 93 per cent, red blood count, 4,960,000, white blood count, 6,500, and the sedimentation time, 55 minutes Blood serum agglutination tests were strongly positive for malta fever in concentrations from 1 640 and 1 160

The temperature curves were irregular for the several observation periods as follows March 1931, for a period of 3 weeks it was between 99 degrees and 101 degrees, June 1931, 99 degrees for 3 days, August, 1931 same for about 6 or 8 weeks, December and January, 1931, and 1932, for 5 weeks the temperature remained between 99 degrees and 100 5 degrees

Recovery followed a course of conservative treatment which was fortified by spinal fusion in August, 1931 Three years later the patient was still symptom free

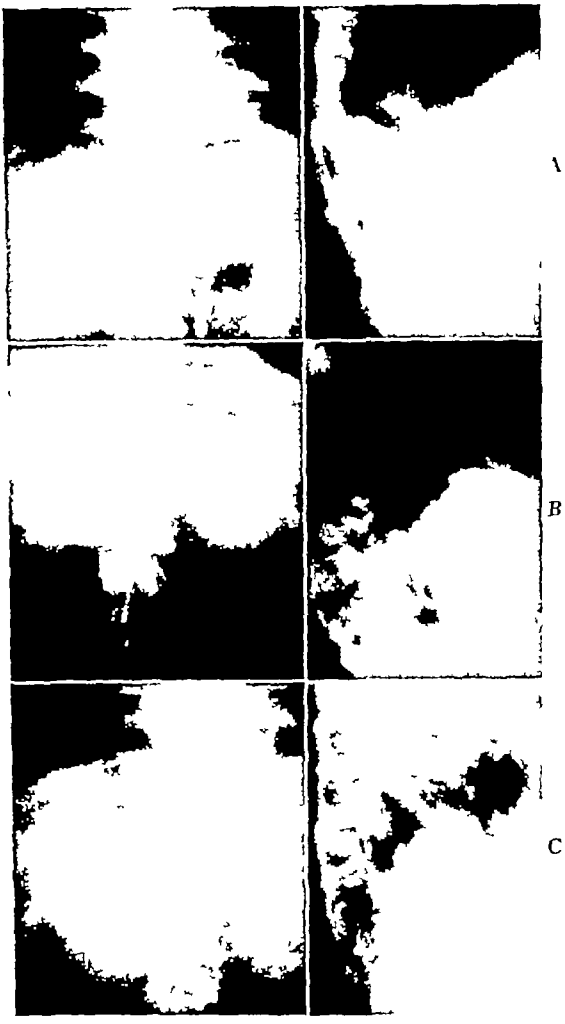

Fig 3 A, March 19, 1931 Anteroposterior view of the lumbodorsal spine shows compression of the twelfth dorsal vertebra There are no signs of abscess formation The lateral view shows compression of the eleventh and twelfth dorsal vertebræ, with erosion of the anterior half of the twelfth superiorly which shows some reaction This resembles fracture strongly but the disc is only slightly narrowed

B, August 5, 1931 Now the disc is practically gone There is osteophytic reaction above and below the site of the lesion The erosive processes are much more pronounced There is now no doubt that the lesion is of an inflammatory nature.

C September 8, 1932 The anteroposterior roentgenogram shows increased condensation and still no evidence of abscess formation The lateral roentgenogram shows definite gibbus formation and the bodies of the eleventh and twelfth dorsal vertebræ are beginning to fuse, as the disc is still more decreased From the posterior aspect the graft appears to be adequately placed and to be solid (Case 2)

FIVE AND TEN YEAR END RESULTS OF THE TREATMENT OF CANCER OF THE CERVIX UTERI BY IRRADIATION

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From the State Institute for the Study of Malignant Diseases, Buffalo, New York, Burton T Simpson M D Director

FROM 1913 to 1929 inclusive, 955 cases of epidermoid carcinoma of the cervix uteri were examined at the State Institute for the Study of Malignant Diseases Eighteen cases were not treated 937 were treated by irradiation.

In presenting such a large series, in order to convey the significance of the result of treatment to those interested, it is necessary to classify the cases in some manner

Numerous observers have endeavored to prognosticate results and group cases by means of grading the biopsy specimens. This should not be overemphasized but, taken into consideration with the amount of anatomical involvement it has, we believe, a distinct scientific value. However to prognosticate on the histology alone does not seem warranted Norris (11) in speaking of this method says "Histologic examination is neither a very practical nor a reliable guide as to either the prognosis or the radiation dosage. It may be of some use in groups, but means little in the individual case" Jonstad and Auer say, "From an analysis of the grading of all the cervical cancers treated by radium from 1917 to 1927 (Barnard Free Skin and Cancer Hospital) it can be concluded that grading alone is of no prognostic value."

We are still of the opinion that grouping cases according to anatomical involvement and the clinical manifestations is more reliable in making a prognosis in the individual case than the histological grading of biopsy specimens alone, as so many factors enter into the obtainment of a good result. Accordingly we have adopted the Schmitz classification and since 1920 we have grouped each case at the time of treatment And although it is undeniable that a personal equation enters into this grouping of cases, we believe it affords a working basis for comparative statistical results

Thirty-eight, or 3 9 per cent of our 955 cases, fell into group I 61 or 6.3 per cent into group II 274, or 28 6 per cent, into group III 456 or 47 7 per cent, into group IV The cases received which were recurrent after hysterectomy were placed in a fifth group and 117 or 12 2 per cent, fell into this group 9 or 0 9 per cent of the cases, were treated prophylactically after hysterectomy

Nearly all of the cases were treated by external irradiation followed by intra-uterine radium as described in a previous paper (15) The results of treatment are given in Tables I and II

In this report no case is included in which there was any doubt as to the malignancy After the biopsy the so called doubtful cases of histological malignancy have been eliminated entirely

In reviewing the number of cases presented here we would like to call attention to the fact that these cases, as classified, show only 10 3 per cent of the cases in groups I and II the cases which might be considered in the operable group that the advanced cases are in the majority 28 6 per cent fell into group III 47 7 per cent into group IV, the hopeless cases

Table III shows a comparison of the type of cases received at the Institute with the types received at other clinics, as reported by various investigators The percentage of group IV cases in our series is considerably higher than from other clinics.

The large number of group IV cases may be explained on the basis that the physicians throughout the State of New York, outside of New York City refer these cases to the Institute while most of the more favorable ones are treated in other clinics The policy of the Institute has been to accept patients for whatever palliation or comfort might be obtained from treatment but ordinarily we believe a great majority of them should have been refused treatment for in this advanced group, 64 8 per cent of the 447 cases treated, died within the first year 42 5 per cent of the 447 died within the first 6 months. Yet, all the cases were included in this statistical report.

At present it seems the consensus is that the result of treatment should be determined from the percentage of survivals of the total cases seen, and we also are submitting our report in this manner

As compared with the absolute statistics (Table IV) from other clinics it will readily be seen that on analysis our percentage of survivals in the first three groups compare very favorably with the results of any of the large cancer clinics However the inclusion of the large number of group IV cases makes the aggregate statistical result somewhat lower for our clinic.

As all investigators are agreed that there is little salvage in the group IV cases, it would seem

TABLE I—FIVE YEAR END-RESULTS[1] OF TREATMENT

Group	Number of cases examined	Number of cases treated	Five year survivals			Five year healings (cured cases)		
			No cases survived	Per cent absolute survivals	Per cent relative survivals	No cases healed	Per cent absolute healings	Per cent relative healings
I	38	37	26	68.4	70 0	24	63 1	64.8
II	61	61	21	34.4	34.4	20	32 7	32 7
III	274	268	55	20 0	20 5	49	17 8	18 28
IV	456	447	7	1 5	1 5	5	1 0	1 1
V	117	115	12	10 2	10.4	12	10 2	10.4
Prophylactic	9	9	3	33 3	33 3	3	33.3	33 3
Totals	955	937	124	12 9	13 0	113	11 8	12

[1]All cases lost from observation or dead from intercurrent disease are counted as dead from the disease.

TABLE II—TEN YEAR END-RESULTS[1] OF TREATMENT

Group	Number of cases examined	Number of cases treated	Ten year survivals			Ten year healings (cured cases)		
			No cases survived	Per cent absolute survivals	Per cent relative survivals	No cases healed	Per cent absolute healings	Per cent relative healings
I	18	18	8	44.4	44.4	7	38 8	38.8
II	39	39	9	23 0	23.0	9	23 0	23.0
III	163	159	13	7 9	8 1	13	7 9	8 1
IV	260	253	0	0	0	0	0	0
V	74	74	10	13 5	13 5	10	13 5	13 5
Prophylactic	6	6	1	16 6	16 6	1	16 6	16 6
Totals	560	549	41	7 3	7.4	40	7 1	7 2

Two of the 18 patients in group I were clinically well for 5 years and 1 was clinically well for 7 years when they died from intercurrent disease with no evidence of malignancy at the time of death

One of the patients in group II was clinically well 9 years and 2 months when she died from intercurrent disease.

Six of the cases in group III passed the 5 year period without any evidence of the disease 3 died from intercurrent disease, 1 after being clinically well for 7 years and 2 after being clinically well for 5 years 2 died from recurrence of their malignancy 1 after being well for 9 years and 1 after being well for 5 years 1 patient was lost from observation after being clinically well for 8 years

[1]All patients lost from observation or dead from intercurrent disease are counted as dead from the disease.

TABLE III—A COMPARISON OF THE TYPES OF CASES RECEIVED IN DIFFERENT CLINICS AS REPORTED BY VARIOUS INVESTIGATORS

Classification	Investigator	Per cent group I	Per cent group II	Per cent group III	Per cent group IV	Per cent group V	Per cent prophylactic
Schmitz	Ward and Sackett (21)—457 cases	2	18 6	69 3	10 1		
	Norris (12)—153 cases	18 9	12.4	37 9	30 7		
	Schmitz (14)—488 cases	7 1	12 7	45.4	34.6		
	Schreiner and Wehr—955 cases	3 9	6.3	28 6	47 7	12	0 9
Individual	Burnam (3)—1578 cases	9 37		61.40 plus 6 27 palliative		19 13	3.8
League of Nations	Crossen and Newell (4)—121 cases	2.4	9	80 1	8 2		
	Lacassagne (10)—350 cases	10.8	37 7	42 5	8.8		
	Heyman (6)—1439 cases	9 8	28	38 7	23 5		
	Voltz (20)—2202 cases	16.8	22.2	36 1	24.7		
	Ward and Sackett (21)—457 cases	20 6	39 2	30 1	10 1		
American College Surgeons	Bartlett and Smith (2)—143 cases (Cases traceable for 5 years)	3.49	7 62	48 2	40 5		

TABLE IV.—COMPARATIVE FIVE YEAR END-RESULTS OF IRRADIATION TREATMENT OF CARCINOMA OF THE CERVIX UTERI

Classification	Investigator	Percentage of survivals or cures							
		Group I	Group II	Group III	Group IV	Group V	Transfer-Recur	Total [illegible] all cases	Total [illegible] groups I, II, & III
Schmitz	Ward and Beckett (11)—457 cases Survivals	[illegible]	[illegible]	[illegible]				[illegible]	[illegible]
	Morris ( )—[illegible] cases Cures	[illegible]	[illegible]	[illegible]	[illegible]			[illegible]	[illegible]
	Schmitz (14)—[illegible] cases Good and results	[illegible]	[illegible]	[illegible]	[illegible]			[illegible]	[illegible]
	Schmitz and Wilde—[illegible] cases Cures Survivals	[illegible]	[illegible]	[illegible]		[illegible]	[illegible]	[illegible]	[illegible] [illegible]
Individual	Bonnier (1)—[illegible] cases Cures	[illegible]		[illegible]		[illegible]	[illegible]	[illegible]	
Lesions of the Cervix	Cramer and Newell (4)—[illegible] cases Survivals							[illegible]	[illegible]
	Lacassagne (10)—[illegible] cases Cures	[illegible]	[illegible]	[illegible]				[illegible]	[illegible]
	*Hayman (8)—[illegible] cases Cure rate—relative absolute—[illegible] cases	[illegible]	[illegible]	[illegible]	[illegible]			[illegible] [illegible]	[illegible]
	*[illegible] (10)—[illegible] cases Cures—relative absolute—[illegible] cases	45	[illegible]	[illegible]	[illegible]			[illegible] [illegible]	[illegible]
American College Surgeons	*Burdick and [illegible] (1)—[illegible] cases Five year survivals for treatable cases	[illegible]	[illegible]	[illegible]	[illegible]			[illegible]	

*Except for these last three investigations, the figures given are absolute

that the thing to do would be to calculate the percentage of survivals from the first three groups for comparative results.

It will be plain to the reader of this statistical paper that results in a curative way by irradiation treatment of cancer of the cervix, will be improved only when these lesions are discovered in the incipient stage when the treatment is quite satisfactory. This will be accomplished only as the knowledge which has been gathered by students of cancer can be disseminated among the lay people as well as among the general practitioners of medicine.

This necessitates periodic health examinations which include a complete physical examination and, in this particular field, careful bimanual pelvic examination together with inspection of the vagina and cervix with a good light, preferably with the colposcope. The use of Lugol solution as advocated by Schiller is of value in detecting areas which are suspicious of malignancy. The areas which do not stain should be selected for biopsy, as after all biopsy is the most important thing in a questionable case.

Emmert, upon reviewing the case histories of patients with advanced disease found "that one-half of the patients claimed they had been under the care of a physician for periods of time ranging from 2 months to 1½ years, during which time the signs of early malignancy were not recognized."

The important steps in cancer prevention are, we believe:

1. The full appreciation of the importance of a periodic health examination which will disclose inflammatory lesions such as cervicitis and erosion, the results of infections and chronic irritations in the endocervix, and the proper treatment of these by means of operative interference and cauterization. Bailey, in his researches which are worthy of careful consideration by all who are endeavoring to prevent malignancy states that the ultimate sequel to erosion is malignancy.

2. The proper and careful attention during pregnancy, delivery and puerperium to prevent lacerations and infections. In our 955 cases only 21 were unmarried women, 97 were nulliparous and in the remainder pregnancies or miscarriages are recorded from one to eighteen times. It is very evident from this fact alone that child bearing with its resulting trauma and the cervicitis (inflammation of cervical glands) or other such chronic inflammations, is a distinct factor in the etiology of cancer of the cervix.

TABLE V —AGES

Age in years	No Cases	Per cent in each age period
20 to 24	8	0 8
25 to 29	30	3 1
30 to 34	63	6 6
35 to 39	94	9 8
40 to 44	146	15 2
45 to 49	151	15 8
50 to 54	155	16 2
55 to 59	150	15 8
60 to 64	81	8 5
65 to 69	46	4 8
70 to 74	21	2 2
75 to 79	7	0 7
80 to 83	3	0 3
Total	955	

Attention is frequently called to the fact that the incidence of cervical cancer is lower in Jewesses Sorsby says "The observance of the Mosaic code undoubtedly produces a high degree of sexual cleanliness, and it is suggested that this cleanliness, with its concomitant restrictions on cohabitation at times when rest is probably beneficial, as after parturition and menstruation, is a factor in the lower incidence of uterine cancer among Jewish women—the regulations of the Mosaic code make the appearance of discharges a cause for inquiry as to its nature and a woman with a blood-stained discharge is theologically 'unclean'" Only one of the patients in our group was Jewish

Kaplan, in reporting the cases examined at the Bellevue Hospital in New York City, says that only 4 per cent of his series were Jewish

3 A realization of the possible dangers that may result from the use of strong chemicals, drugs, instruments, and instrumentation, sometimes used as contraceptives

Parabuceu, quoted by Stout, collected data from several Russian gynecological clinics which show that cancer of the uterus in women from 24 to 30 represents no less than 24 per cent of all cases of uterine cancer He attributes this to the increasing use of artificial abortion and anticonceptional methods in Russia

4. A full realization that cancer of the cervix may occur at any age period in life as is indicated in reviewing the age table (Table V)

From this table it will be seen that cancer of the cervix has occurred in every period in adult life, the youngest being 20 and the oldest being 83, that there is a gradual and perceptible increase in the percentages in each 5 year period up to the maximum of 55, and then a decline In our series (16) 4 9 per cent occurred at age 30 or younger Johnson and Tyrone report 6 5 per cent under the age of 30

The duration of symptoms for our cases was about the same for all groups, from a few weeks to several years, 632, or 66 1 per cent of the patients, complained of bleeding as their first symptom, 126, or 13 1 per cent, of a discharge, either watery, yellowish, leucorrheic, or greenish, 123, or 12 6 per cent, as a watery discharge which later became bloody, 53 of pain or pressure symptoms with no discharge, 7 were discovered on routine physical examination, 14 gave indefinite histories Pain accompanying symptoms was found in the advanced cases From this, we conclude that there is not much to be learned of the extent of the disease from the symptoms

Abnormalities of the menstrual function, prior to the beginning of the present complaint, were found in only 159 of the cases, 102 patients reported painful periods, 30 irregular periods, 23 irregular and painful periods, 3 severe headaches, and 1 patient reported irregular periods and nose bleeds

Ninety-five, or 9 9 per cent, of these women gave positive Wassermann reactions Touraine, in the study of 29 cases of leucoplacia of the cervix in which syphilis was present clinically in 66 per cent, found 12, or 41 per cent, terminated in epithelioma

Nothing of any consequence was learned from a study of the nationality in our series, except that there was only one Jewess among 955 patients

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EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

FRANKLIN H MARTIN, M D
Founder and Managing Editor
1905–1935

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APRIL, 1936

WILLIAM H WILMER

WITH sorrow the Editorial Staff of SURGERY, GYNECOLOGY AND OBSTETRICS has learned of the death of one of its most honored members, Dr William H Wilmer

As a surgeon, a leader in the field of ophthalmology, and a citizen, he has long been a distinguished figure in American life Dr Wilmer's career was characterized by many fruitful accomplishments In a subsequent number the Journal will give more adequate recognition to his achievements

THE SURGEON'S DEBT TO FUNDAMENTAL SCIENCE

THE time is not far removed when a surgeon achieved eminence by the development of brilliant, dexterous, and rapid technical procedures during an operation While such skill must still be an asset to the surgeon, yet if not accompanied by the knowledge and appreciation of the biochemical, physiological, and psychological disturbances inseparable from all disease processes, the results of such surgical procedures will leave much to be desired Such an individual is merely an operator, a technician, carrying out stereotyped procedures—not a surgeon

The training of a surgeon has now become so complicated that the former presumably adequate knowledge of anatomy and surgical pathology must be supplemented by a training in biochemistry and physiology To these sciences we are deeply indebted

If obstruction occurs in any hollow tube of the human organism, the resultant disaster in all instances is hastened by the associated biochemical upset A dexterous but precipitate operation to relieve an obstruction in the small bowel, colon, common bile duct, ureter, or urethra will result in a discouraging mortality if the biochemical disturbances are neglected and left untreated as shown by the knowledge provided through research experiments conducted by the fundamental sciences

How often a precipitate operation in a septic patient ends fatally The patient may be overcoming the initial focus and localizing it as a relatively innocuous abscess, but most frequently the price of such a victory is exhaustion from pain and sleeplessness, dehydration, and a change in ratio of circulatory fluids, salts, and solids, the net result being an organism with a completely disturbed metabolism and an embarrassed circulation

If the associated disturbances are corrected before an operation is undertaken, the de-

lightful improvement of patients suffering from the lesions mentioned is well-nigh incredible. The most obvious and easily corrected are pain and dehydration, with the inevitable disturbance of the acid base balance. The intravenous administration of saline and glucose in large quantities, often thousands and not hundreds of cubic centimeters, is required to restore the balance of the circulatory fluids. Morphia gives mental and physical rest.

When the improvement in the patient's condition has reached a stage where an operation is possible it should be of the most simple character dealing solely with the lesion responsible for the disability From the physiological and biochemical laboratories has come evidence of the necessity of decompression of a distended viscus prior to any extensive operative procedure. Examples of the practical application of the above principle are found in a cecostomy for obstruction due to cancer of the colon a cholecystostomy or draining of the common bile duct in empyema of the gall bladder or cholangitis, or decompression of the urinary bladder when urethral obstruction follows prostatic enlargement. Such procedures are not directed to the correction of the actual organic lesion causing the disability they are directed to correcting the physiological and biochemical upsets resulting from such a lesion By these minor procedures the patient is rescued from a severe crisis, and the radical procedure necessary to attack the primary organic lesion may be carried out with safety at a later date It would be disastrous to do a radical operation on a patient for a cancer of the colon when the patient really is suffering from intestinal obstruction

The application of the above principles to patients suffering from acute perforation of a duodenal ulcer has permitted us to operate on forty consecutive patients without a death. Sixteen of these patients required subsequent radical operation. None died from this secondary procedure. The time consumed in carrying out such pre-operative preparation is more than justified by the ultimate results.

For this attitude to clinical problems we are indebted to the fundamental sciences. The more "biologically minded" a surgeon becomes, the lower will be his mortality the less will his patients suffer mental and physical anguish during and subsequent to their surgical therapy ROSCOE R. GRAHAM.

PERITONITIS FOLLOWING COLONIC SURGERY

USUALLY peritonitis following intestinal operations is attributed to (1) contamination at the time of the surgical procedure or (2) infection which develops subsequently because of impairment of the vascular supply of the segment of bowel. While improvement in operative technique has unquestionably diminished the occurrence of peritonitis, it nevertheless still remains one of the outstanding postoperative complications of abdominal surgery

Peritoneal infection may be expected if, at operation, contamination of gross character has taken place but when it occurs following a surgical procedure in which there has been no soiling and no obvious technical error it is a tragedy Older contemporary surgeons have observed repeatedly that peritonitis develops with comparative rarity following secondary abdominal operations, provided the primary procedure has been carried out only 2 or 3 weeks previously For example, peritonitis is quite uncommon following closure of a colonic stoma subsequent to segmental resection of the colon, and the conjecture is made that its failure to develop is due to immunization that has been brought about by the primary opera-

tion and the presence of the stoma If this statement even in part is correct, the feasibility of attempting immunization against peritonitis arises

Some feel that the use of vaccine in an attempt to prevent peritonitis following colonic operations is useless, others believe that it is dangerous Progress in medicine must be made cautiously and slowly, but many find it difficult to accept any new idea simply because it deviates from the paths of tradition The attempt to vaccinate patients who are to undergo operation on the colon is not new in principle, Mikulicz attempted it many years ago The vaccine he used contained colon bacilli which had been killed The occurrence of some severe reactions discouraged him and he discontinued the use of the vaccine During the past 2 or 3 years Gosset has administered vaccine subcutaneously prior to abdominal operation in an effort to decrease the incidence of peritonitis, and he is of the opinion that it is of considerable value The work of Steinberg and Goldblatt also lends evidence to the contention that vaccination is apparently a preventive therapeutic measure against infections of the peritoneum

In the past 7 years more than 2 500 intraperitoneal injections of vaccine have been made at the Mayo Clinic as a preventive measure against peritonitis in cases requiring intestinal operations The vaccine is made from killed streptococci and colon bacilli The amount of vaccine usually employed in each case was 1 cubic centimeter (500,000,000 organisms) in 10 cubic centimeters of physiologic saline solution as a diluent However, for patients of small stature and for children, smaller doses were administered Vaccination is carried out by means of a long spinal puncture needle after the abdominal site has been carefully prepared and the area anesthetized by the use of procaine In addition to the vaccine, which is given 48 to 60 hours prior to operation, all patients are hospitalized for 3 to 5 days before operation During this period an effort is made to cleanse the bowel as thoroughly as possible without increasing the debilitation of the patient Stated briefly, the procedure consists in the employment of a diet high in carbohydrate and the use of mild saline cathartics If the bowel is obstructed or nearly obstructed, warm saline irrigations are substituted for cathartics All of the 2,500 patients who were given the vaccine underwent some type of intestinal operation subsequently, and in the interim since the institution of this plan of pre-operative preparation, the mortality from peritonitis following intestinal surgery has decreased 66 per cent

According to recent experience, it would seem that the dangers of intraperitoneal vaccination can best be summarized by stating that there has not been an alarming reaction or death that could be attributed to the use of the vaccine Intraperitoneal vaccination is not projected as a sure preventive against infection, but the principle is fundamentally sound and the employment of the vaccine seems to be a step in the right direction

CLAUDE F DIXON

LANDMARKS IN SURGERY

OLIVER WENDELL HOLMES AND PUERPERAL FEVER

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It rarely happens that a man is fortunate enough to acquire merited distinction in two entirely unrelated fields of human endeavor A physician who acquired this distinction is Oliver Wendell Holmes. The average American layman thinks of Oliver Wendell Holmes as the author of a wide variety of literary gems, especially the *Autocrat of the Breakfast Table*. Most Americans do not know that Holmes was a physician and a professor of anatomy for 35 years However as Holmes himself said, he made far greater contribution to humanity as a physician than as an author and poet. Many physicians have become literati but, as Osler pointed out, they did so at the expense of acquiring distinction in the field of medicine. Holmes was a rare exception for he became famous both in medicine and in literature

Oliver Wendell Holmes did not start his educational career studying medicine Instead he began the study of law at the Harvard Law School but after one year he gave this up and turned to medicine. After graduating from medical school he went abroad where he came under the influence of a number of prominent teachers Bearing in mind the famous French physician Louis, he said, "I have fully learned three principles since I have been in Paris, not to take authority when I can have facts not to guess when I can know not to think a man must take physic because he is sick Throughout his entire life Holmes never forgot these three principles

After his return to America Holmes began the practice of medicine, but if the number of patients he had and the income he derived from them are used as criteria Holmes was not a successful physician He knew this better than any one else and as he himself said, "A man who writes poetic ditties must not write prescriptions To be a wit was bad enough to be a poet, worse Better be a rascal or hard drinker and have some bond of sympathy with your few patients" However Holmes was eminently successful from every point of view as a teacher For 35 years Holmes was professor of anatomy at the Harvard Medical School In the early years Holmes taught not only anatomy but also physiology and he had so many duties to perform that he was led to make the following oft-repeated statement, "Instead of filling a chair at the University I really occupy a settee." Although the teaching of anatomy is difficult to make interesting and although Holmes lectures were given at the time of day when most students were fatigued, the students were always eager to attend these lectures. Holmes was famous as the greatest conversationalist in America for he talked better than he wrote. He had a delightful sense of humor and this, coupled with his extensive knowledge of anatomy and his familiarity with the history of the great anatomists, made Holmes' lectures inspiring Holmes was always interested in old books on medicine and collected a large number of them which are now in the Boston *Medical Library* It may also be of interest to know that Holmes wrote the greatest number of poems dealing with medical subjects in the English language. Among these are such well known poems as "Rip Van Winkle M D" and "The Stethoscope Song

Oliver Wendell Holmes
1809–1894

In 1843 Holmes read a paper on "The Contagiousness of Puerperal Fever" before the Boston Society for Medical Improvement. This paper was published in the *New England Quarterly Journal of Medicine and Surgery* in April, 1843, but it aroused very little comment because of the limited circulation and life of the journal in which it was published. Holmes stoutly maintained that puerperal fever was not only contagious but that it was communicated by the doctor either directly or indirectly He said, "The disease known as puerperal fever is so far contagious as to be frequently carried from patient to patient by physicians and nurses." Holmes made the following rec-

ommendations "A physician holding himself in readiness to attend cases of midwifery should never take any active part in postmortem examinations of puerperal fever cases A physician present at such postmortems should use thorough *ablution*, change every article of dress and allow 24 hours to elapse before attending a case of midwifery Similar precautions should be taken after the autopsy or surgical treatment of cases of erysipelas if the doctor is obliged to unite such duties with his obstetrical work which is in the highest degree inexpedient"

It was natural that such a damning indictment of the medical profession should sooner or later arouse opposition Surely enough, a few years after Holmes' paper appeared, Hodge, who was professor of obstetrics at the University of Pennsylvania, and later Meigs, who was professor of obstetrics at the Jefferson Medical College, took strong exception to Holmes' statements and abused him personally These two obstetricians were the leading authorities on obstetrics in the United States at the time and *therefore their comments carried a great deal of* weight with the doctors of this country Holmes replied to the bitter criticisms leveled at him by reprinting his original article and giving new data to support his beliefs He chose the following significant title for his second paper, "Puerperal Fever As a Private Pestilence" This paper demonstrates Holmes' masterful control of English, his clear and logical reasoning, and his generosity in giving credit to his predecessors who contributed to the subject of puerperal fever In spite of the acrimony which characterized Hodges' and Meig's criticisms, Holmes maintained a reserved dignity and restraint of temper in his reply After the publication of Holmes' second paper, many physicians accepted Holmes' ideas

During the last few years there has been a great controversy as to who was the first to discover the cause of puerperal fever An investigation of practically all great scientific discoveries will reveal that it is extremely rare for one man to make a significant scientific discovery alone without depending upon advances made by his predecessors or his contemporaries Usually one man is given the credit for a great discovery, but it is generally the one who describes it most clearly and who persists in writing or talking about it until it is accepted Puerperal infection has undoubtedly existed as long as mankind References to it have been made by many ancient writers, but the English term puerperal fever is credited to Strother who used it in 1718 However, in 1676 Willis spoke of "febris puerperarum" which is the Latin equivalent

In discussing the discoverers of the cause of puerperal fever, credit in this country is generally given to Oliver Wendell Holmes, whereas on the continent abroad, Semmelweis is accorded the honor of being the discoverer However, the contagious nature of puerperal fever was known to Charles White in 1793, to Alexander Gordon in 1795, to Denman in 1801,

Contagiousness of Puerperal Fever 503

ART V —*The Contagiousness of Puerperal Fever* Read before the Boston Society for Medical Improvement, by OLIVER W HOLMES, M D , and published by request of the Society

IN collecting, enforcing and adding to the evidence accumulated upon this most serious subject, I would not be understood to imply *that there exists a doubt in the mind* of any well-informed member of the medical profession as to the fact that puerperal fever is sometimes communicated from one person to another, both directly and indirectly In the present state of our knowledge upon this point I should consider such doubts merely as a proof that the sceptic had either not examined the evidence, or, having examined it, refused to accept its plain and unavoidable consequences. I should be sorry to think with Dr Rigby, that it was a case of "oblique vision," I should be unwilling to force home the *argumentum ad hominem* of Dr Blundell, but I would not consent to make a *question* of a momentous fact, which is no longer to be considered as a subject for trivial discussions, but to be acted upon with silent promptitude. It signifies nothing that wise and experienced practitioners have sometimes doubted the reality of the danger in question, no man has the right to doubt it any longer No negative facts, no opposing opinions, be they what they may or whose they may, can form any answer to the series of cases now within the reach of all who choose to explore the records of medical science.

If there are some who conceive that any important end would be answered by recording such opinions, or by collecting the history of all the cases they could find in which no evidence of the influence of contagion existed, I believe they are in error Suppose a few writers of authority can be found to profess a disbelief in contagion—and they are very few compared with those who think differently—is it quite clear that they formed their opinions on a view of all the facts, or is it not apparent that they relied mostly on their own solitary experience? Still further, of those whose names are quoted, is it not true that scarcely a single one could by any possibility have known the half or the tenth of the facts bearing on the subject which have reached such a *frightful amount within the last few years*? Again, as to the utility of negative facts, as we may briefly call them,—instances, namely, in which exposure has not been followed by disease, —although, like other truths, they may be worth knowing, I do not

Facsimile of title page of paper entitled "Contagiousness of Puerperal Fever"

to Armstrong in 1814, and to many other Englishmen long before Holmes and Semmelweis even thought about this disease. According to Peckham, the first American physician to write on the subject of puerperal fever was David Hosack of New York who said that puerperal fever was not infrequently highly contagious In spite of the fact that these physicians recognized the contagious nature of puerperal fever, Holmes and Semmelweis fought hard to convince the medical profession of the truth of this Holmes' efforts were almost entirely limited to his pen, but Semmelweis fought hard battles in his effort to convince his colleagues of the contagiousness of puerperal fever He gave a clear definition of the disease showing conclusively that it is an infection of the genital wounds, he collected valuable clinica land pathological data, he gave experimental proof, and he showed the great value of prophylaxis He fought bitterly to overcome the prejudices

against him and finally became insane. In spite of the fact that Semmelweis' first contribution did not appear until 1847 whereas Holmes' first paper was published in 1843 much more credit is generally given to Semmelweis for his efforts in spreading the truth about puerperal fever than to Holmes.

Holmes' essays on puerperal fever as well as Semmelweis' contributions, were eventually fully accepted by the medical profession and resulted in an enormous reduction in the number of maternal deaths throughout the entire civilized world. Late in life Holmes said that his essays on puerperal fever gave him much more satisfaction than the poetry and prose he wrote throughout his long *life*. Among other statements concerning this, he said "When by the permission of Providence, I held up to the professional public the damnable facts connected with the conveyance of poison from one mother's chamber to another for doing which humble office I desire to be thankful that I have lived, though nothing else shall ever come to life I had to bear the sneers of those whose position I had assailed. "

Holmes died peacefully at the age of 85 having retained the full vigor of his mind until the end His loss was mourned not only by those interested in medicine and in literature, but also by all who were interested in the welfare of womankind. Throughout the world mothers have every reason to revere the memory of Oliver Wendell Holmes

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

A FORMIDABLE work[1] by Weiss and collaborators on diseases of the liver, biliary tract and pancreas consists of 1099 pages, printed on glossy paper and well illustrated with many photographs, diagrams, and X-ray plates, from the author's own and others' cases There is an extensive list of references, covering 166 pages, and a subject and author's index. It is by far the most pretentious monograph by an American author that has appeared on the subject. In general it follows the influence of the German school, it is largely clinical, lacking perhaps in the presentation of the known fundamental physiological facts concerning the liver, bile ducts, gall bladder, and pancreas, required for a thorough understanding of the diseases of these organs from the point of view of the clinician It is a "practical book," designed for the use of the medical student and practitioner, "devoted to the consideration of every day problems in biliary and pancreatic disease."

One chapter is devoted to the "indirect examination of the liver" by means of liver function tests, one to the examination of biliary tract contents after the manner of Lyon, one to the roentgenological examination of the organs considered, and one to the surgery of the liver, gall bladder, and bile ducts The chapter devoted to parasitic diseases of the liver and gall bladder is, indeed, very well done and beautifully illustrated The chapter on jaundice fails to clarify our understanding of the subject despite explanations, an involved classification, and a table of differential diagnosis of hematogenous and hepatogenous jaundice Catarrhal jaundice, after the German style, is presented as a disturbance due to "catarrh" of the bile passages secondary to that of the gastro-intestinal tract This origin is conceivable but now believed very rare But scant attention is paid to the conception of catarrhal jaundice as a mild or abortive hepatitis involving the parenchymatous cells of the liver, which recent study would indicate is most frequently present

The use of the term "portal hypertension," to which condition the author devotes a chapter, is interesting and unique That a condition of hypertension exists within the portal system, similar to but independent of general arterial hypertension, as implied, is interesting if true Most clinicians think of the condition described in terms of portal obstruction or stasis

On the whole the volume is an interesting, instructive, comprehensive compilation on diseases of the liver, bile ducts, gall bladder, and pancreas, which will be appreciated by many practitioners

CHARLES A. ELLIOTT

THE impressive tome of 1581 pages—*Agents of Disease and Host Resistance*[2] by Gay represents a large and comprehensive undertaking Part I, which may be regarded as an introduction to the book and an exposition of the author's concept of the cause of disease, treats of the general aspects of the causation, classification, and nature of disease Part II deals with inanimate disease, agents as trauma, temperature, light, chemical poisons, etc., the tolerance of the organisms to them and the subjects anaphylaxis and allergy. Part III traces the history of bacteriology particularly in relation to disease and discusses the nature, form, structure, and physiology of micro-organisms and infection Part IV covers infection in general and the principles of epidemiology Part V has to do with resistance and immunity including a chapter on tissue immunity by the senior author whose research in this field is extensive and valuable Part VI describes in detail the pathogenic bacteria and the diseases produced by them, Part VII the pathogenic spirochetes and spirochetoses, and Part VIII the pathogenic fungi and fungus diseases Part IX under the heading "Indeterminate Pathogenic Forms and the Diseases Produced by Them" takes up the Rickettsia and filterable viruses with a chapter on the bacteriophage Part X deals with the animal agents of disease the protozoa, helminths, and arthropods Part XI is devoted to the diseases of obscure etiology which constitute approximately one-third of the total number of known diseases Part XII discusses the practical application of bacteriological and immunological diagnostic reactions, active immunity through recovery and vaccination, serum prophylaxis and serum therapy and chemotherapy of bacterial and protozoan infections From this outline, the breadth of scope and the fact that the contents of the book involve many branches of medicine is apparent

The method of approach differs from the conventional in that instead of placing emphasis on particular agents or agencies the many agents together with the various secondary factors and host response

[1] DISEASES OF THE LIVER, GALL BLADDER DUCTS AND PANCREAS THEIR DIAGNOSIS AND TREATMENT By Samuel Weiss, M D., F A C P Chapter on SURGERY by J Prescott Grant, M.C. F.A.C S , M R.C.S Chapter on ROENTGENOLOGY by A. Judson Quimby M D., F.A.C.R. New York. Paul B Hoeber, Inc. 1935

[2] AGENTS OF DISEASE AND HOST RESISTANCE, INCLUDING THE PRINCIPLES OF IMMUNOLOGY, BACTERIOLOGY, MYCOLOGY, PROTOZOOLOGY, PARASITOLOGY AND VIRUS DISEASES. By Frederick P Gay and collaborators Springfield, Illinois, and Baltimore, Maryland Charles C Thomas, 1935

are correlated and integrated to form a broad background for the presentation of disease causation. For the intimate knowledge required for the many phases of such an enterprise, the author is fortunate in the contributing authors all of whom, with the exception of four have been associated with him in the same department. This has maintained better balance and continuity. Attention is centered on principles rather than practice, consequently detailed technical procedures are almost entirely omitted. The book is intermediate between a text book and a system or collection of monographs. It is predicted that the volume will have an extensive use among specialists in infectious diseases, teachers, investigators, and practitioners and among graduate students. However general medicine should find the book interesting and profitable, particularly Part I. The book is a rich mine of information.

A. A. Day.

THE sixth edition of *Preventive Medicine and Hygiene*[1] has been extensively rewritten and entirely reset. Many new subjects—such as contraception, maternal mortality, heart disease, diabetes, ringworm, snake bites, and pellagra—have been added for the first time in this book. The discussions of venereal diseases, sex hygiene, heredity and eugenics, drug addiction, vitamins and the deficiency diseases, infant mortality, industrial hygiene and diseases of occupation, scarlet fever and enteric fever have been extensively revised. Changed opinions have been withdrawn and each subject rewritten. The author has largely reorganized and added much new material to the subjects of tuberculosis, diphtheria, Vincent's angina, measles, insect borne diseases, ticks, quarantine, etc. The purpose of this, as of previous editions, is to meet the demand for an authoritative treatise based upon modern progress in hygiene and sanitation.

The book may be considered in two parts: first, that part which deals with the individual, and second, that part which deals with the environment of the individual.

The author's many years of varied experience in public health work, combined with the contributions of various authors in particular subjects, gives this book the authoritative scientific basis from which can be secured accurate knowledge in the effort to prevent disease and maintain health.

Clifford J. Barnett.

[1] Preventive Medicine and Hygiene. By Milton J. Rosenau. 6th ed. New York and London: D. Appleton-Century Co., 1936.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

A Glasgow Manual of Obstetrics. By Samuel J. Cameron, M.B., F.R.F.P.S., F.C.O.G., John Hewitt, M.B., Ch.B., F.C.O.G., Robert A. Lennie, M.D., F.R.F.P.S., F.C.O.G., Ellen D. Morton, M.B., Ch.B., M.C.O.G. 3d ed. London: Edward Arnold & Co., 1936.

A Textbook of Obstetrics, for Students and Practitioners. By Frederick C. Irving, A.B., M.D., F.A.C.S. New York: The Macmillan Co., 1936.

The Physiology of Life: a Radio-Electric Interpretation. By George Cole. New York: W. W. Norton & Co., Inc., 1936.

Oxford Medical Publications. The Tuberculosis Handbook. By Halliday Sutherland, M.D. London: Oxford University Press, 1936.

La Endocrinología en España. By Dr. Angel Guerraro Abellan. Barcelona, Spain, 1936.

Those Were Good Days! By Carl Ludwig Schleich. Translated by Bernard Miall. New York: W. W. Norton & Co., 1936.

A Textbook of Roentgenology: The Roentgen Ray in Diagnosis and Treatment. By Basil J. Michael Harrison, M.B., Ch.M., D.M.R.E. (Cantab.), F.A.C.R. Baltimore: William Wood & Co., 1936.

Post-Graduate Surgery. Edited by Rodney Maingot, F.R.C.S. (Eng.). With an Introduction by The Rt. Hon. Lord Moynihan of Leeds, K.C.M.G., C.B., M.S., F.R.C.S. Vol. 1. New York: D. Appleton-Century Co., Inc., 1936.

An Introduction to Surgery. By Rutherford Morison, M.D., F.R.C.S. Edin., F.R.C.S. Eng., M.A., D.C.L., LL.D. and Charles P. M. Scott, C.B.E., M.D., M.S., F.R.C.S., F.R.A.C.S. 3d ed. Baltimore: William Wood & Co., 1935.

The Teen Physician: The Modern Doctor of the Old School. By Wingate M. Johnson, M.D. New York: The Macmillan Co., 1936.

A Textbook of Surgery. By American Authors. Edited by Frederick Christopher, B.S., M.D., F.A.C.S. Philadelphia and London: W. B. Saunders Co., 1936.

An Index of Differential Diagnosis of Major Symptoms. By Various Writers. Edited by Herbert French, C.V.O., C.B.E., M.A., M.D. Oxon., F.R.C.P. Lond. 4th ed. Baltimore: William Wood and Co., 1936.

AMERICAN COLLEGE OF SURGEONS

LIBRARY AND DEPARTMENT OF LITERARY RESEARCH, AMERICAN COLLEGE OF SURGEONS

IRVIN ABELL, M D, F A C S, LOUISVILLE, KENTUCKY
Chairman, Committee on the Library

THE gradual, well-rounded development of the Library of the American College of Surgeons and the many calls upon its facilities on the part of the Fellows of the College and other members of the medical profession is a source of gratification to the Committee on the Library The Library, established with the well-chosen collection of the late John B Murphy as a nucleus, has been augmented during the past fifteen years by additional interesting and valuable collections Outstanding among these are the volumes from the Albert J Ochsner collection of bound journals and textbooks, presented through the courtesy of the Augustana Hospital, and the volumes of historic interest which, together with the pictures and mementoes of his life and work, were placed in the Albert J Ochsner Memorial Room by the late Mrs Ochsner

The William McDowell Mastin and the H Winnett Orr collections likewise contain volumes of historic interest The former is especially rich in eighteenth and nineteenth century monographs and the latter, consisting of approximately four hundred volumes, includes a rare Galen (1633), a Paré (1579), Boerhaave's *Opera Omnia Medica Complectentia*, and other museum pieces A catalogue of the Orr collection is being prepared by the donor and will undoubtedly prove an interesting and valuable historical study in the field of general and orthopedic surgery

Many individual volumes and smaller collections have been received from time to time Dr G P Coopernail has presented a small volume, *Sententiae Omnes*, by Francisco Venerio (1555), a volume containing the handwritten notes to the third edition of Emmet's *Principles and Practice of Gynaecology*, and the pamphlet entitled *Dr Wells, the Discoverer of Anaesthesia* Among the present day studies are to be found the beautifully illustrated limited editions by Nolie Mumey entitled *William Beaumont the Centenary of the Publication of His Contributions to Medicine* and *Silas Weir Mitchell the Versatile Physician*

The more extensive contributions to the general reference library include the journal files of the late Albert Van der Veer and the unique, fifty-volume collection of the late H W Mills on hydatid cysts The reference library likewise contains an extensive and valuable collection of current textbooks and monographs, and representative surgical journals of the world, American, Canadian, British, Australian, Mexican, South American, and Continental, which, together with the collections available through neighboring university and private libraries, makes possible the research service offered by the Department of Literary Research

Many are accustomed to think of a library only in terms of immediate availability to personal visitation, desirable as this opportunity may be the lack of it does not interfere with the acquisition of data and knowledge comprised in the world of surgical literature The staff of the College Library welcomes both the personal visits of the Fellows and, as well, their requests by mail or wire for specific material in which they may be interested

The staff of workers maintained to care for these requests is equipped to select material of interest from the extensive reprint files (package library service) and to compile bibliographies, prepare abstracts and translations on any medical or surgical subject The package library file includes approximately 90,000 pamphlets and permits of a prompt response to each request, data being furnished within a few hours' time if need be However, the package library does not afford a complete review of a subject When a complete study is desired the package library should be supplemented by a bibliography and translations of the important articles upon the subject, with notes or brief abstracts of those of lesser interest. The Department of Literary Research, maintaining on its staff workers trained in this field, is well

equipped to furnish this more complete service. The personnel includes full-time workers experienced in translating from the German, French, Italian, Spanish, Dutch and Scandinavian languages and associated workers in the Bohemian Russian, and Hungarian languages. It is thus prepared to meet practically any language requirement which may arise. Brochures descriptive of the plan of the Department, and blanks to facilitate the placing of inquiries are furnished upon request.

Today the research field marks the zone of advance in the development of surgical knowledge, its gleanings being harvested by the laboratory worker and the clinical observer For the vast majority of surgeons engaged in private practice as are the Fellows of the College, clinical research and priority achievement constitute the greatest means of adding to the sum total of surgical attainment. A complete bibliography prepared by the Department of Literary Research with abstracts and translations of all articles presented in the polyglot literature of the world is a study of great value to such persons. An analysis will reveal similar or comparable experiences, the value of laboratory data, the opportunity of comparing pathological findings, the contrast of diverse treatments with therapeutic results, and a more or less correct evaluation of all the clinical factors. A study conducted along such lines acquires a definite value and an accredited position in surgical literature and the Department of Literary Research has spared no pains in making its program along this line both helpful and complete

It is the hope of the Committee on the Library that Fellows of the College and other members of the profession will continue in increasing numbers to take advantage of the facilities which the Library offers to the end that one of the objectives of the College namely, increase in and dissemination of surgical knowledge may be more widely attained. The Library is the property of the Fellows of the College and a sense of possession should stimulate them to use it to their own advancement In so doing they would be conscious of raising the level of surgical practice and adding to the Science and Art of Surgery

THE 1936 CLINICAL CONGRESS IN PHILADELPHIA

FOR the twenty-sixth annual Clinical Congress of the American College of Surgeons to be held in Philadelphia, October 19–23, 1936, the surgeons of that great medical center have organized under the leadership of a strong and representative committee, and are planning to provide a program of surgical clinics and demonstrations that will present a complete showing of their clinical activities in all departments of surgery The Executive Committee in charge of arrangements is as follows Henry P Brown, chairman, Gilson C Engel, secretary, Francis H Adler, Dorothy C Blechschmidt, John O Bower, L K Ferguson, Bruce L Fleming, Karl M Houser, Robert H Ivy, H P Leopold, Richard H. Meade, Jr , Frank Mogavero, John R Moore, E A Mullen and Louis C Scheffey The Committee is assured of the hearty co-operation of the clinicians at the five medical schools and more than thirty hospitals that will participate in the clinical program

A preliminary schedule of operative clinics and demonstrations is being prepared by the Committee for publication in an early issue of SURGERY, GYNECOLOGY AND OBSTETRICS Clinics will be arranged for the afternoon of Monday, October 19, and for the mornings and afternoons of each of the four following days All departments of surgery will be represented in the program—general surgery, gynecology and obstetrics, genito-urinary surgery, neurosurgery, orthopedics, proctology, and surgery of the eye, ear, nose and throat.

The Executive Committee of the Board of Regents is preparing programs for the five evening sessions At the presidential meeting on Monday evening, the first formal session of the Congress, the retiring president, Dr Donald C Balfour, will deliver his address The president-elect, Dr Eugene H Pool, will deliver his inaugural address at the convocation on Friday evening, on which occasion the 1936 class of initiates will be received into Fellowship At sessions on Tuesday, Wednesday, and Thursday evenings eminent surgeons of the United States and Canada together with visiting surgeons from foreign countries will present and discuss papers dealing with surgical subjects of timely importance

In addition to an extensive schedule of operative clinics and demonstrations at the hospitals, the sub-committee on ophthalmology and otolaryngology is preparing a series of clinical demonstrations to be held daily in the ballroom of the Bellevue-Stratford Hotel to be given by visiting ophthalmologists and otolaryngologists

The Committee on Arrangements expects to emphasize certain special features in the clinical program including (1) fracture clinics, demonstrating modern methods in the treatment of fractures, (2) cancer clinics, demonstrating the treatment of cancer by surgery, radium and X-ray, (3) clinics in traumatic surgery for the presentation of the newer methods of rehabilitation of the injured by surgery and physical therapy

Other features of this year's Congress include a conference on fractures under the auspices of the Committee on Fractures, a cancer symposium arranged by the Committee on the Treatment of Malignant Diseases, and a conference on industrial medicine and traumatic surgery under the auspices of the Committee on Industrial Medicine and Traumatic Surgery

The showing of films demonstrating clinical features of interest has met with popular acceptance in recent years and will be continued at this session with an enlarged program of surgical films, both sound and silent, to be exhibited daily at headquarters

Following its established custom and in recognition of an obligation to the public to provide authoritative information on modern surgery, better hospitals, and the prevention of disease, a community health meeting will be held Wednesday evening in the Municipal Auditorium under the auspices of the College

The annual hospital conference will open the Congress with a session in the ballroom of the Bellevue-Stratford Hotel at 10 o'clock on Monday morning An interesting program of papers, round table conferences, and practical demonstrations dealing with problems related to hospital efficiency is being prepared for sessions on Monday, Tuesday, Wednesday, and Thursday A greatly increased interest on the part of surgeons in both the administrative and scientific phases of hospital work has been evidenced in recent years and the program of this year's conference will provide for discussions of subjects of interest to the three major hospital groups—medical, surgical, and administrative It is proposed to make this year's program of wide interest and practical character through a careful selection of subjects to be presented and discussed by surgeons and hospital executives, particular emphasis being directed toward professional standards

and the vital problems related to hospital economics

Headquarters for the Congress will be established at the Bellevue-Stratford Hotel where the grand ballroom, Garden Clover and Red Rooms and other large rooms on the first and second floors have been reserved for scientific sessions and conferences, registration and clinic ticket bureaus, bulletin boards, executive offices, etc. Thus the activities of the Congress will be centralized under one roof

The Technical Exhibition will be located in the large rooms on the first and second floors adjacent to the ballroom. The registration and clinic ticket bureau, together with the information desk, will be centrally located as regards the exhibit rooms in which will be placed the bulletin boards on which the daily clinical program will be posted each afternoon. Leading manufacturers of surgical instruments, X-ray apparatus, operating room lights, hospital apparatus and supplies of all kinds, ligatures, dressings, pharmaceuticals and publishers of medical books will be represented in this exhibition.

We are assured that the railways of the United States and Canada will grant reduced rates for the Clinical Congress in Philadelphia, and negotiations for such fares are in progress with the various railway traffic associations.

The hospitals and medical schools of Philadelphia afford accommodations for a large number of visiting surgeons, but to insure against overcrowding, attendance at the Congress will be limited to a number that can be comfortably accommodated at the clinics, the limit of attendance being based upon the result of a survey of the amphitheaters, operating rooms, and laboratories of the hospitals and medical schools to determine their capacity for visitors. It is expected, therefore, that those surgeons who wish to attend the Congress will register in advance.

Admittance to clinics and demonstrations will be controlled by means of special clinic tickets, such plan providing an efficient means for the distribution of the visiting surgeons among the several clinics and insuring against overcrowding, as the number of tickets issued for any clinic will be limited to the capacity of the room in which that clinic is given.

A registration fee of $5 00 is required of each surgeon attending the annual Clinical Congress, such fees providing the funds with which to meet the expenses of the meeting To each surgeon registering in advance a formal receipt for the registration fee is issued, which receipt is to be exchanged for a general admission card upon his registration at headquarters This card, which is non-transferable, must be presented in order to secure clinic tickets and admission to the evening meetings.

SURGERY, GYNECOLOGY AND OBSTETRICS

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THE INTRAVENOUS USE OF HYPERTONIC GLUCOSE IN OBSTETRICS AND GYNECOLOGY

AN EXPERIMENTAL AND CLINICAL STUDY[1]

HARVEY B MATTHEWS, M D, F A C S, AND VINCENT P MAZZOLA, M D, F A C S, BROOKLYN, NEW YORK

ONE of the most confusing syndromes encountered in all branches of medicine is shock This syndrome is generally recognized to be a group of symptoms and not a disease (1, 2, 4) It is used to denote a condition of acute peripheral circulatory collapse It does not resemble cardiac decompensation, as it lacks the characteristic signs of edema, visceral congestion, and accumulation of fluids in the serous cavities The more common predisposing causes of surgical shock are the following (1) acute hemorrhage, (2) trauma of extensive wounds, (3) prolonged anesthesia, (4) excessive manipulation of abdominal viscera during operation, while those of obstetrical shock are (1) acute antepartum and postpartum hemorrhage, dehydration and acidosis, (2) the severe toxemias of pregnancy, (3) extensive trauma of difficult delivery, and (4) prolonged anesthesia Two types of shock resulting from injury and/or loss of blood may be recognized (1) primary shock or collapse in which the low blood pressure follows immediately and (2) secondary shock, in which the development of low blood pressure is delayed Surgeons are most frequently confronted with this latter type while obstetricians most usually encounter the former

In spite of much research on this subject, the actual causes of the disturbances in circulatory function are still unknown Many theories have been advanced as to the cause of shock, but no uniformity of opinion exists as to its production Likewise, different opinions are held regarding its treatment However, we do know that in shock there is a stasis of blood in the periphery, a sharp reduction in circulating blood volume, and a consequent fall in blood pressure (2, 3) It therefore follows that any treatment of this shock like state must increase circulating blood volume and blood pressure An increased blood pressure with no increase in blood volume is undesirable But an increase in blood volume which naturally increases the blood pressure is highly desirable

In this connection we may mention the action of vasomotor drugs Although such drugs temporarily increase the blood pressure, they actually diminish the quantity of blood reaching the organs The temporary rise in blood pressure is never sustained For example, adrenalin produces a more prolonged increase in the blood pressure and in the output of the heart than the other drugs commonly used for this purpose However, it is a well known fact that a normal animal can be placed in a state of shock by the frequent introduction of large amounts of adrenalin When continued vasoconstriction is produced without increasing blood volume, the amount of blood reaching the organs is decreased rather

[1] From the Departments of Physiology and Obstetrics and Gynecology, Long Island College of Medicine and the Department of Obstetrics and Gynecology Methodist Episcopal Hospital.

than increased. A lack of oxygenation of tissues results, producing further damage. Likewise other vasomotor drugs cause similar reactions.

The ideal method of treatment is to introduce some fluid into the blood stream that will cause an increase both in blood volume and blood pressure. To accomplish this result, blood and its substitutes have been employed. Whole blood is the ideal therapeutic agent for increasing the blood volume and blood pressure. It is universally agreed that the best method of treating shock due to hemorrhage is by transfusion of whole blood. When whole blood is used there is a dilution of red blood cells in the blood stream due to the passage of fluid from the tissue spaces back into the blood vessels. Whole blood therefore will increase blood volume although, when injected intravenously in the presence of circulatory stasis, protein is lost through the capillary walls. This, however is at least partially compensated for inasmuch as a very large amount of additional protein is being put into the circulation by the intravenous injection of blood.

As an emergency measure, in the actual absence of blood or because of delay in obtaining the proper donor it is usually necessary to use a substitute for blood in order to tide the patient over this critical waiting period. The results following the use of most of the substitutes have not been very encouraging. Isotonic saline (5 9) has been shown to be of little practical value It will temporarily cause an increase in blood pressure, but as the fluid injected passes into the tissue spaces, the blood pressure will in a very short time, be as low as before and usually lower Besides, with the injection of normal salt solution there is a decrease in the total amount of plasma and at the same time a decrease in the percentage of protein in a unit volume of plasma. Therefore, isotonic saline will not cause an increase in the volume of blood in the circulation because with the diminished osmotic pressure only a diminished quantity of fluid is attracted back into the blood vessels from the tissue spaces *Weak solutions of glucose have proved to be no more efficient.* Solutions of acacia and gum acacia with glucose have their adherents (6 13) but accidents have been reported (8) following their use.

From the diversity of opinions, it is therefore apparent that the perfect substitute for blood has not been found. Perhaps it will never be found, but we all agree that emergency measures at times are necessary for the preservation of life. Since the value of the introduction of large quantities of fluid into an already impaired circulation during shock is questionable we have attempted *to produce the desired results (i e., increase the volume in the circulation and raise the blood pressure) by diminishing the volume of the infusion and increasing its concentration.*

Experimentally (10, 11 12) two groups of animals (cats[1]) were studied (1) a group in which shock with low blood pressure was artificially produced by *hemorrhage*, and (2) a group in which it was produced by *trauma* without hemorrhage. From this study we found that the injection of 50 per cent glucose into cats with artificially reduced blood pressure produced a characteristic reaction in all cases. There was always a rise in blood pressure, an increase or a return to the original pulse pressure, and a slowing or a return to the original pulse rate. In group 1 the cats had received glucose previous to bleeding and they reacted to hemorrhage much better, at least from the standpoint of blood pressure, than did those cats that had not received glucose, the final pressure level being much closer to the previous normal. The administration of glucose after hemorrhage always increased the pulse pressure. The final pulse pressure was closer to the original when glucose had been given previous to the hemorrhage than in those cases where no initial glucose was given (Figs. 1 and 2) These findings would indicate that the diminished blood pressure, the rapid pulse, and the fall in pulse pressure subsequent to hemorrhage in the experimental animal can be combated, at least in part, by the intravenous injection of 50 per cent glucose solution. If hemorrhage is anticipated and a fortifying dose of 50 per cent glucose solution is given the bleeding produces far less effect on the circulation than would otherwise be encountered

[1] The cats for each group were used. [illegible] with a very different amount of blood were required and the effect of 50 per cent glucose noted. Likewise for the trauma group

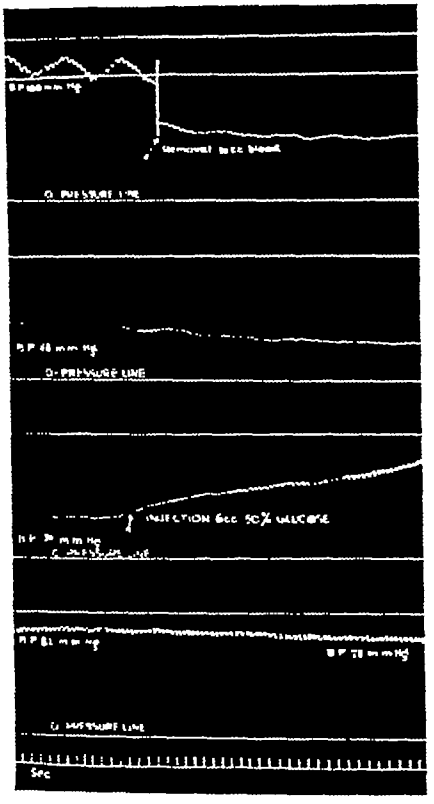

Fig 1 Response following the injection of 6 cubic centimeters of 50 per cent glucose after removal of 30 cubic centimeters of blood. Note immediate rise of blood pressure after injection of 50 per cent glucose.

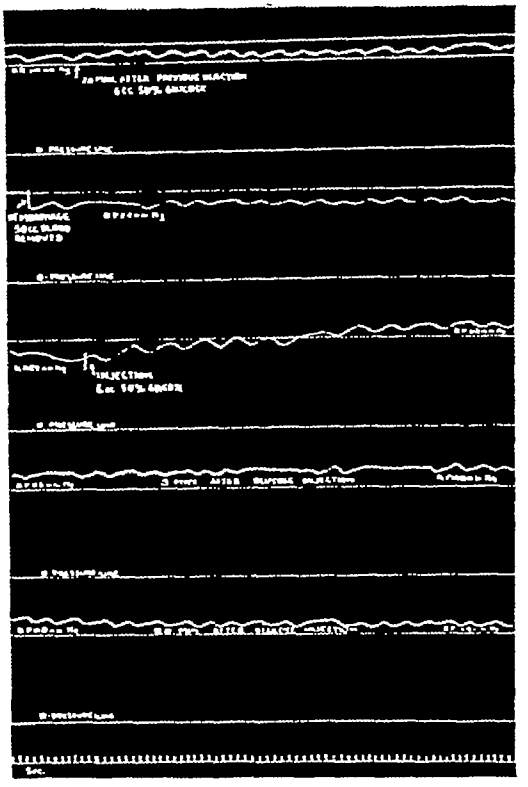

Fig 2 Response following the injection of 6 cubic centimeters of 50 per cent glucose after removal of 50 cubic centimeters of blood, 6 cubic centimeters of 50 per cent glucose having been given previous to withdrawing the 50 cubic centimeters of blood. Note that blood pressure is maintained more near its original normal.

In group 2, injections of 50 per cent glucose in the cats (those with an artificially reduced blood pressure by trauma without loss of blood) produced a characteristic reaction in all cases There was always a rise in blood pressure, an increase or a return to the original pulse pressure, and a slowing or a return to the original pulse rate The initial degree of fall in blood pressure, upon the release of the tourniquet following trauma, was about the same whether glucose had been previously given or not But when a fortifying dose had been given, there was the tendency for the blood pressure to rise again subsequent to the trauma The sustained fall in blood pressure, in this series, was less than the fall in the animals without the previous injection of glucose Hence the final maintained blood pressure level was much higher after trauma when glucose had been previously given The pulse rate in all cases was slowed after the injection of glucose (Figs 3, 4, and 5)

These findings would indicate that the low blood pressure and the rapid pulse subsequent to trauma can be temporarily, at least, successfully combated by the intravenous injection of 50 per cent glucose Furthermore, if a fortifying dose of 50 per cent glucose be given the cat before trauma is performed, the subsequent fall in blood pressure and acceleration of the pulse is finally maintained more near the normal or above it than when no previous glucose is given

CLINICAL DATA

We are living in an era of preventive medicine Any therapeutic agent, therefore, that will prevent or help to prevent, or that will

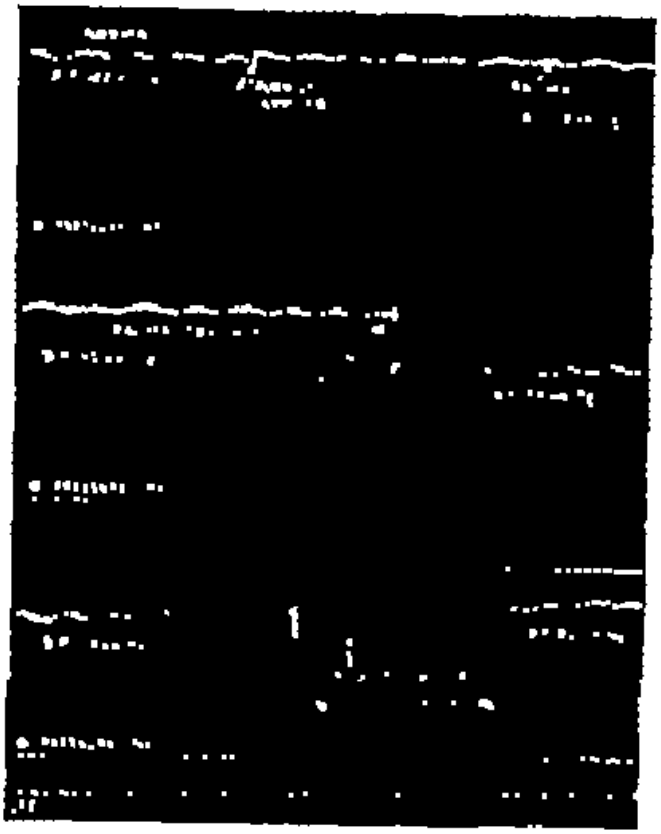

Fig. 3. Response following injection of 6 cubic centimeters of 50 per cent glucose after trauma, i.e. injury to left leg. Note sharp fall in blood pressure upon removal of tourniquet from injured leg. Further, note rise in blood pressure after injection of 6 cubic centimeters of 50 per cent glucose.

relieve or help to relieve, a given pathological lesion is worthy of our serious consideration. Glucose is such a therapeutic agent. In fact glucose may be designated the "universal therapeutic agent" for it has many and varied uses in general medicine, pediatrics, surgery and obstetrics and gynecology.

Regarding the general usefulness of glucose the physiologists tell us that:

1. It is a food for the vital organs especially the liver and heart muscle.

2. It requires no digestive processes to prepare it for absorption; being a monosaccharide it is spontaneously and completely metabolized to carbon dioxide and water.

3. Its use temporarily improves the quality of the pulse by improving the ventricular filling of the heart.

4. It temporarily raises the systolic blood pressure and produces a peripheral circulation by its osmotic effect on tissue fluids.

5. It promotes diuresis and combats acidosis.

6. It temporarily lowers body temperature.

7. It increases the protective power of the blood and, according to Hofbauer, it stimulates the production of myelocytes.

8. It increases the coagulation time in jaundiced patients but increases the clotting time in other patients.

9. In high concentration it prevents agglutination of the blood and in diabetics glucose and insulin promote glycogen storage in the heart.

From extensive laboratory and clinical research we know that the ideal intravenous solution in the treatment of shock and its allied conditions should act (1) to increase blood volume in the cardiovascular system without overloading the heart, (2) to provide easily accessible nourishment for the tired out myocardium and liver—i.e. replacement of glycogen in these organs, (3) to help restore the circulation in general, and (4) to tide the patient over the critical period of shock, dehydration and acidosis, profound toxemia, and critical infections until transfusion and other suitable therapeutic measures can be instituted. Furthermore, it would seem that the intravenous addition of large quantities of fluid of any nature, except perhaps blood, is inadvisable and often actually dangerous for it might very well mean the addition of an insurmountable load on an already impaired circulation and weakened myocardium, which might result in cardiac dilatation and failure (14).

Fearing, therefore, the use of large quantities of fluid intravenously in "shocked cases" we have, during the past 6 years, used from 50 cubic centimeters to 200 cubic centimeters of 50 per cent solution of glucose (dextrose) (usually 100 c. cm.) with excellent results. In those cases in which acute shock was not the primary indication for the use of glucose, 300 cubic centimeters of a 25 per cent solution in saline has been employed. Some cases have received these glucose injections before and after operation and during labor merely as a prophylactic measure while others received them for postoperative and post partum complications. Hypodermoclysis of normal saline is usually given immediately following the intravenous glucose in sufficient

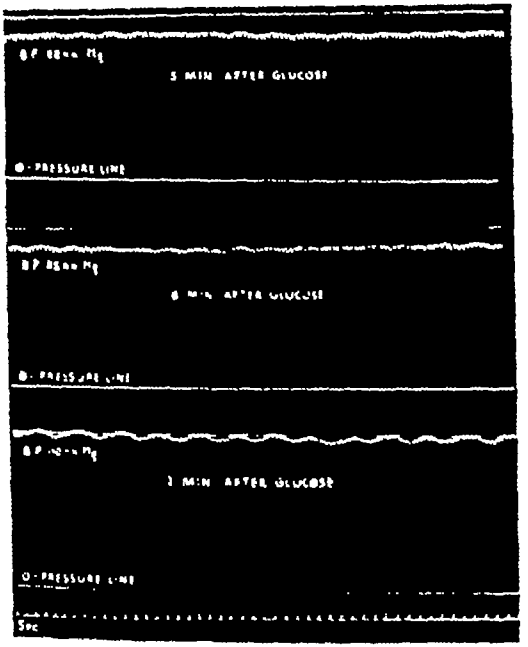

Fig. 4. Continued (Fig 3) response to injection of 6 cubic centimeters of 50 per cent glucose

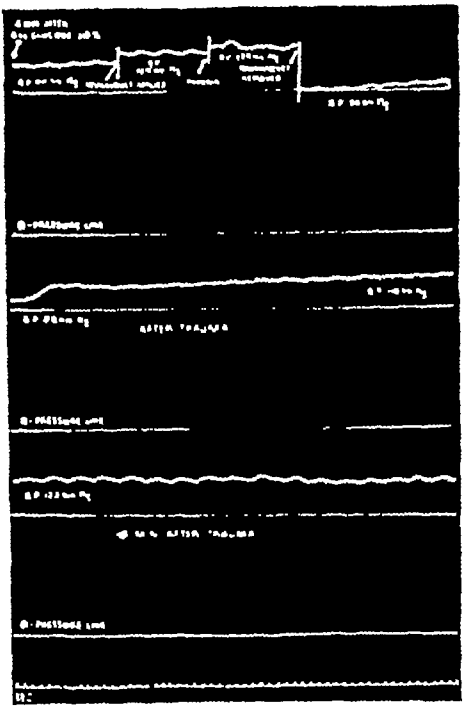

Fig 5 Response to trauma after injection of 6 cubic centimeters of 50 per cent glucose Note blood pressure after application of tourniquet was released Note also the gradual improvement in blood pressure after trauma, due to previous administration of 50 per cent glucose.

quantity to supply the required fluid (water) i e, 2000 to 5000 cubic centimeters per 24 hours

Cases of fatigue showing venous stasis, hypotension, leucopenia, dry tongue, and the general picture of lack of circulatory tone are poor operative risks besides being good subjects for subsequent thrombosis with fatal embolism Injections of hypertonic (50 per cent) glucose will not only improve the cardiac tone and increase the blood pressure, but will also help in preventing intravenous clotting On the contrary, cases with hypertension have greatly improved with routine rest and hypertonic glucose solution Blood pressure in these cases has shown marked improvement and hence the patient is better prepared for operation

Prolonged labor produces muscle fatigue which is shown by the gradual increase in pulse rate, slowing of uterine contractions, tendency of the tongue to become dry, intestinal distention and usually some rise in temperature The tired parturient patient is a poor operative risk Furthermore, anesthesia upsets the balance between the constituents of the protein radicle which has already been disturbed by the pregnancy In such cases a dose of morphine secures both physical and uterine rest, and an intravenous injection of 50 to 100 cubic centimeters of 50 per cent glucose solution will completely change the patient's appearance as the pulse is slowed and both the systolic and pulse pressures are improved The reaction to 100 cubic centimeters 50 per cent glucose in 25 cases was typical and is illustrated graphically in Chart 1

In cases of acute antepartum hemorrhage (ablatio placentæ, placenta prævia), abortion, postpartum hemorrhage and tragic ectopic gestation, the introduction of 50 to 100 cubic centimeters of a 50 per cent glucose solution will raise the blood pressure from 15 to 50 millimeters of mercury within a period of 5 to 10 minutes This rise is maintained from 20 to 45 minutes which gives sufficient time to prepare for transfusion The rapidity and duration of the effect is proportionate to the quan-

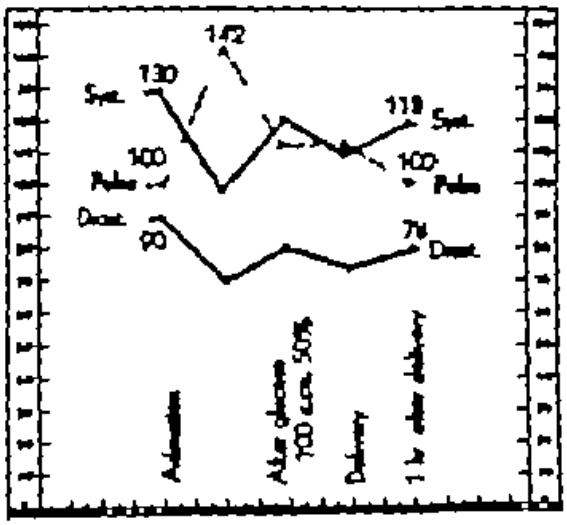

Chart 1 Reaction to glucose, 50 per cent, 100 cubic centimeters, in prolonged labor.

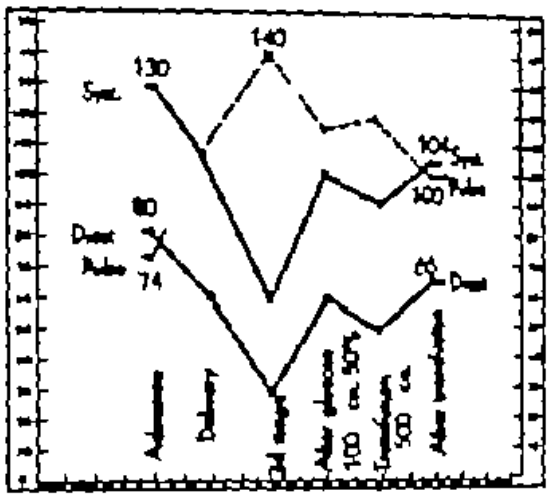

Chart 2 Reaction to glucose, 100 cubic centimeters, 50 per cent, in postpartum hemorrhage

tity of glucose injected. The reaction was typical in each group as illustrated in Charts 2 3 4 and 5

Goltz, in 1863 demonstrated that a blow on the exposed mesentery of a suspended frog caused a reflex inhibition of the heart action through the vagus and lessened the vascular tone throughout the body especially in the abdominal cavity This primary shock or collapse has been observed in obstetrics in a few cases of postpartum hemorrhage where, for its control the uterus was lifted out of the pelvis and forcibly compressed against the spinal column (posterior wall) We have had 6 such cases in which there was severe shock following a moderate loss of blood due to the partial separation of the normally implanted placenta. In all, the picture has been typical a clear mentality excessively low systolic pressure, terminal cyanosis, and general vasomotor collapse In each case, intravenous injection of 100 cubic centimeters of a 50 per cent glucose improved the condition sufficiently so that transfusion speeded the woman on to recovery A typical reaction is illustrated in Chart 6

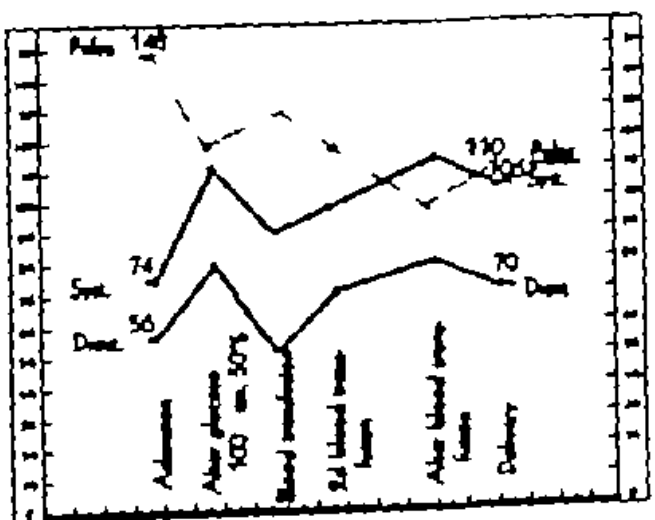

Chart 3 Reaction to glucose, 100 cubic centimeters, 50 per cent, in placenta previa.

In a recent case of complete vaginal plastics for prolapsus of the uterus with marked rectocele and cystocele, while traction was being made on the cervix and the anterior cul-de-sac opened the patient suddenly went into shock. She became pulseless, bathed in cold perspiration and the systolic pressure fell from 140 to 40 millimeters of mercury No diastolic pressure could be recorded Within 6 minutes after the introduction of 100 cubic centimeters of a 50 per cent solution of glucose the radial pulse could be counted, the systolic pressure rose to 110 and continued to rise during the next half hour to 130 and was maintained at this level.

As a prophylactic measure, we have found that the intravenous injection of 100 cubic centimeters of hypertonic 50 per cent glucose prior to operation makes reduction of blood pressure from loss of blood trauma of operation, and prolonged anesthesia of less frequent occurrence. A group of 100 laparotomies for fibroids, adnexal disease, and retroversions, were studied in which 100 cubic centimeters of hypertonic 50 per cent glucose

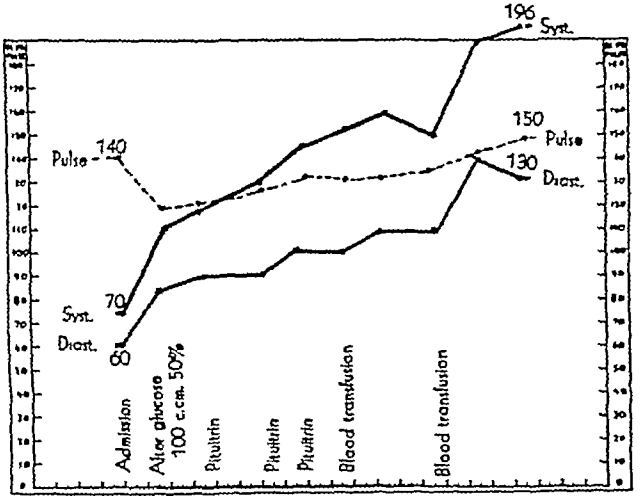

Chart 4 Reaction to glucose, 100 cubic centimeters, 50 per cent, in ablatio placentæ

had been given prior to operation The final systolic blood pressure after operation was better maintained and nearer the normal. Chart 7 illustrates the average reaction in this series A similar group of 100 laparotomies was studied in which no preliminary glucose had been given In this group, there was always a constant reduction of systolic and diastolic blood pressure The average fall in this series was 12 millimeters of mercury The pulse rate showed an average increase of 20 beats per minute Chart 8 illustrates the typical reaction

In the postoperative routine carried out in most hospitals it is the custom to use large quantities of normal saline solution by enteroclysis or by hypodermoclysis The efficiency of this addition of chlorides can be materially augmented by improving the circulatory action by the intravenous instillation of concentrated glucose solutions Postoperatively we have used intravenous injections of 300 cubic centimeters hypertonic (25 per cent) glucose with 2000 cubic centimeters of normal saline by hypodermoclysis routinely in several hundred cases In some cases we have repeated the glucose and saline two or three times A detailed study of this routine in 100 laparotomies revealed an increase in systolic blood pressure of 8 to 10 millimeters of mer-

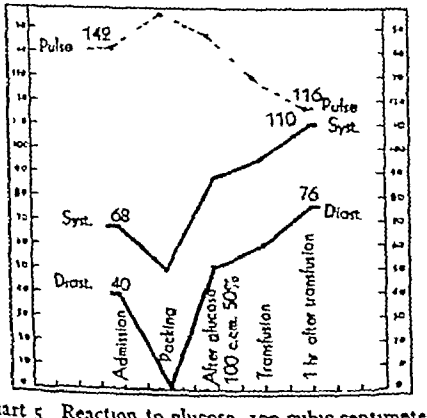

Chart 5 Reaction to glucose, 100 cubic centimeters in incomplete abortion with severe hemorrhage.

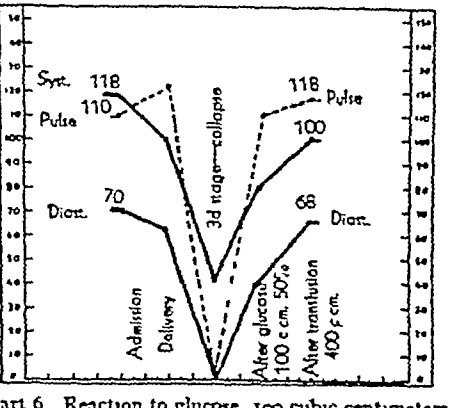

Chart 6 Reaction to glucose, 100 cubic centimeters, 50 per cent, in postpartum circulatory collapse.

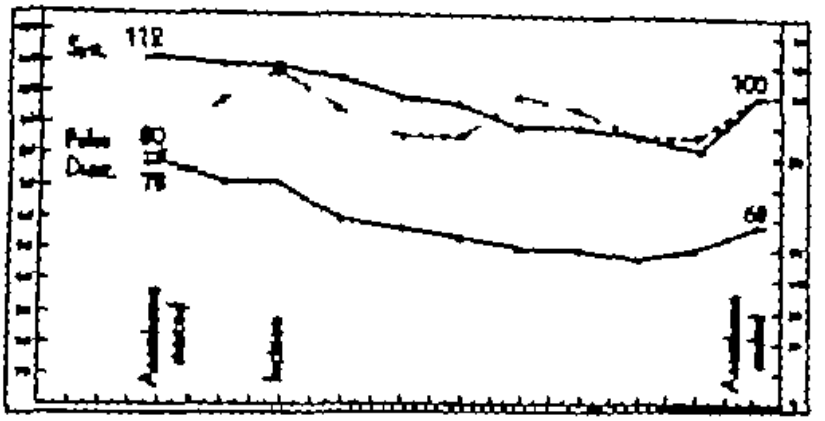

Chart 8 Operative reaction in 100 laparotomies with no previous glucose

cury The pulse rate showed a tendency to become slower Chart 9 gives the typical reaction to postoperative glucose and saline. The postoperative reactions of diminished blood pressure and pulse pressure with elevation of pulse rate epigastric distention, and vomiting have been less encountered. Acidosis and dehydration were not as common A comparative study as shown in Chart 10 demonstrates these findings in 564 cases in which this routine was followed

SUMMARY

Experimentally the findings indicate that the diminished blood pressure, the rapid pulse and the fall in pulse pressure, subsequent to hemorrhage or trauma in the experimental animal, can be combated at least in part by the intravenous injection of 50 per cent glucose. When hemorrhage or prolonged trauma is anticipated a fortifying dose of 50 per cent glucose lessens the depressing effect on the circulation to a considerable degree.

Clinically in cases of hypotension intravenous 50 per cent glucose with routine preoperative rest, gives the patient a wider margin of safety for operation The hazards of prolonged labor have been diminished by the intravenous use of hypertonic glucose. Cases of acute hemorrhage with diminished blood pressure have shown increase in blood pressure by the intravenous injection of 100 cubic centimeters of 50 per cent glucose. It tides these patients over until blood transfusion can be started For primary shock or collapse hypertonic (50 per cent) glucose increases systolic blood pressure and greatly aids in bringing the circulation back. Pre-operative glucose makes reduction of blood pressure from hemorrhage or prolonged surgery more difficult After operation it aids in overcoming acidosis and dehydration By its action on the circulation normal saline administered

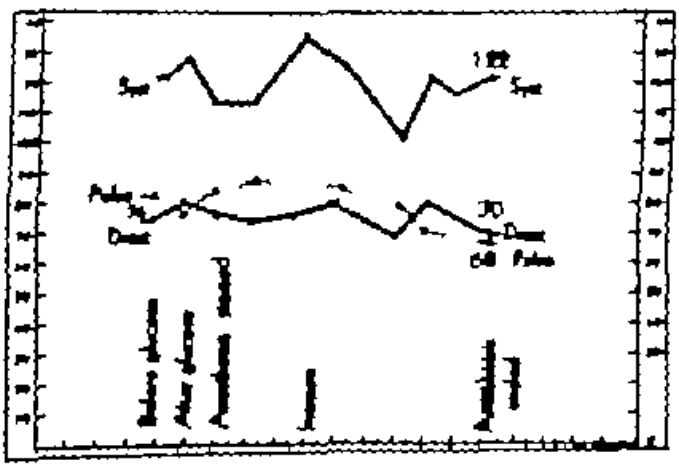

Chart 7 Operative reaction in 100 laparotomies with glucose 100 cubic centimeters 50 per cent administered previous to operation

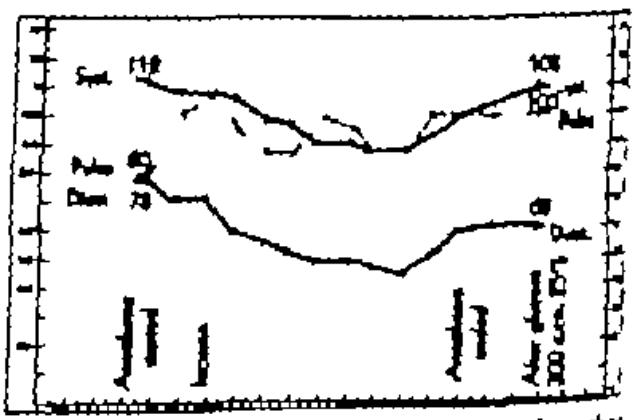

Chart 9 Operative reaction in 100 laparotomies with no previous glucose but with 500 cubic centimeters, 50 per cent, after operation

by hypodermoclysis is more readily absorbed It also aids in supplying carbohydrates when the oral route is contra-indicated We have not observed reactions following the intravenous administration of hypertonic (50 per cent) glucose We hold no brief for glucose as a substitute for whole blood in hemorrhage or in shock, or in the exhausted patient, but experience has taught us that in shock with or without hemorrhage, it is to be commended Active treatment must be instituted before there is complete circulatory collapse The patient who receives prompt treatment is the one who recovers When blood is not available or when time is pressing, concentrated glucose solution makes an excellent substitute We can say with all positiveness that concentrated glucose is a valuable adjunct to pre-operative preparation It maintains pulse pressure causes a slight rise in systolic blood pressure and, if repeated, prevents a fall It diminishes postoperative vomiting and has considerable value as a food in the presence of peritoneal infection

Little or no damage is done the vein by injections of hypertonic glucose (50 per cent), provided the intima of the vessel is not excessively traumatized We have used the same vein repeatedly without trouble

CONCLUSIONS

From this study the following conclusions may be drawn

1 Fifty per cent glucose injected intravenously into cats with a reduced blood pressure produces a final sustained rise in blood pressure and pulse pressure and a diminution in pulse rate

2 Preliminary injections of hypertonic glucose (50 per cent) make reduction of blood pressure by hemorrhage or trauma more difficult

3 Secondary shock, dehydration, and acidosis are, to a great extent, preventable in the routine work in obstetrics and gynecology and the proper use of hypertonic intravenous glucose plays a most important rôle in their prevention as well as in their relief

4 In acute hemorrhage or injury followed by shock with marked reduction of blood pressure, intravenous hypertonic glucose will raise the blood pressure and thus tide the patient over until transfusion can be given

CHART 10 —POSTOPERATIVE REACTIONS

	No P O glucose	With 300 c.cm 25% glucose
Number of laparotomies	500	564
Systolic blood pressure	Average fall 14 mm Hg	Average fall 6 mm Hg
Pulse	Average rise 18 per min	Average rise 8 per min
Vomiting	More common	Less common
Distention	More common	Less common
Acetonuria	More common	Less common

5 During the antepartum and postpartum periods when shock from hemorrhage and/or trauma, fatigue from prolonged labor, dehydration, acidosis, or infection occur, intravenous hypertonic glucose will slow the pulse, raise the blood pressure, help to relieve the acidosis, dehydration, and intestinal distention, and thereby improve the general condition of the patient

6 In the pre-operative preparation of the patient glucose by mouth or better hypertonic intravenous infusion, is a most valuable adjunct in that it helps in fortifying the patient against the hazards of shock coincident with anesthesia and trauma of operation, particularly in major operations in which considerable time is likely to be consumed

7 After operation hypertonic glucose aids in combating dehydration and improves the circulation, helps to control vomiting, assists in the reduction of intestinal distention, and supplies food for the vital organs (4 1 calories per gram)

8 In the treatment of shock and its allied conditions, active treatment must be instituted before there is complete circulatory collapse The patient who receives prompt treatment is the patient most apt to recover

9 The ease of administration of intravenous glucose makes it available for every physician everywhere, since it can be administrated by any doctor who can introduce a needle into a vein—whether in the home, in the office, or in the hospital

10 The commercial ampule form of glucose solutions for intravenous injections now available are free from harmful ingredients, do not

cause untoward reactions, and are therefore apparently perfectly safe

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THE CONTROL OF MORBIDITY AND MORTALITY FOLLOWING PELVIC SURGERY[1]

A Review of a Second Series of One Thousand Consecutive Personal Cases

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SIR D'ARCY POWER has aptly said "There are three stages in the career of a surgeon In the first he loses the fear of hemorrhage, in the second he ceases to multiply operations, in the third he acquires the moral courage to stop in the middle of an operation when he finds the condition inoperable There is a final stage which he never attains with the present span of life, the ability to gauge correctly the vital resistance of the patient, yet on this depends the success of every operation "

In a previous communication[2] I made a critical analysis of 1000 consecutive personal operative cases immediately preceding January 1, 1930, with the following summary and conclusions

In a series of 1000 consecutive gynecological operative cases, there were complications during convalescence in 79, a morbidity of 7 9 per cent, 19 patients died, a mortality of 1 9 per cent

Postoperative transfusion should never be necessary except in the presence of ectopic pregnancy, secondary hemorrhage, or sepsis

Pre-operative cystoscopy and renal function tests will eliminate many useless pelvic operations

Severe anemia, pyorrhea, respiratory affections, a compromised myocardium, arterial hypertension, and impaired metabolism, are indications for postponing operation in elective cases, spinal anesthesia may reduce the hazards in emergency cases

Radiation and diathermy are dangerous in the presence of active infection or necrobiosis

Meticulous peritonealization and burying all suture knots minimizes the likelihood of postoperative intestinal obstruction

The incidence of pulmonary complications can be lessened by the invariable employment of a skilled anesthetist.

Correcting indicanuria and obstinate constipation before operation will practically eliminate postoperative pyelitis

Persuading the patient to practice active motion of the extremities throughout convalescence is good insurance against thrombophlebitis and embolism

Pronounced tachycardia developing during the first half hour of anesthesia is an indication to terminate the operation as soon as possible

Unpreventable surgical shock will develop occasionally in profoundly septic patients

Patients with a high metabolic rate should not be subjected to radiation

Since the publication of the prior series of cases (designated hereafter as Series A) another group of 1000 (identified as Series B), has been completed and I now presume to compare the end-results with the purpose of indicating how each operator may reduce postoperative morbidity and mortality by scrutinizing the details of successive groups of his own cases Both groups serving as the basis for this presentation include patients admitted to my ward service at the New York Post-Graduate Hospital, as well as private patients No patient was denied surgical relief solely because of an unfavorable prognosis I am convinced that personal cases only should be utilized for evaluating the caliber of the pre-operative study and preparation of the patients, and to ascertain whether or not the morbidity was as low as it should have been, and whether or not any of the fatalities could have been avoided It is far more profitable to criticize ourselves than others

Individualities can never be standardized and there are bound to be factors involved in the treatment of patients by different members of the same hospital staff Personal experiences are much more enlightening than the array of a large mass of statistical data taken from the records indiscriminately We can teach others operative technique, but we cannot endow them with dexterity, we can inculcate surgical judgment, but we cannot assure its exercise, and we can outline the principles of postoperative treatment, but the responsibility for their application must always devolve upon the one in actual attendance upon the patient Hence, I believe that it is unfair to appropriate another's successes or include his failures in the assay of a series of end-results

[2] Dannreuther Walter T The control of morbidity and mortality following pelvic surgery Surg., Gynec. & Obst., 1930, 51 522

[1] From the Department of Gynecology, New York Post-Graduate Medical School and Hospital, Columbia University Read before the Central Association of Obstetricians and Gynecologists, Omaha, Nebraska, October 10–12, 1935.

Since most gynecological operations are elective rather than emergent there is usually ample opportunity for thorough pre-operative preparation of the patients. The assurance of metabolic activity fortified vital resistance and mental placidity in each one when she reaches the operating table is an objective just as important as dexterous surgical technique. On the other hand, over enthusiastic pre-operative measures, such as starvation, dynamiting the intestinal tract with drastic purgatives, and a justifiable apprehension on the part of the patient undoubtedly contributed materially to the discouraging morbidity and mortality in the statistics of the pioneers in pelvic surgery. Toleration of anesthetic agents and operative trauma decreases in direct proportion to impairment of physiological processes. The test of good judgment is not the survival of the patient, but an uneventful convalescence.

TABLE I.—MORBIDITY AND MORTALITY

	Series A	Series B
Consecutive gynecological cases	1000	1000
Postoperative complications	79	53
Morbidity per cent	7.9	5.3
Deaths	19	8
Mortality per cent	1.9	0.8

Comparing the two groups, it is apparent that I succeeded in effecting a 34 per cent reduction in morbidity and a 57 per cent reduction in mortality. Of course, a few patients in both series had multiple complications, so that the incidence of complications is slightly higher than the morbidity percentage.

TABLE II.—POSTOPERATIVE COMPLICATIONS

	Series A	Series B
Gastro-intestinal	20	6
Pulmonary	7	1
Wound	16	1
Urinary	2	9
Cardiovascular	1	9
Systemic	7	4
Postoperative hemorrhage	3	4
Miscellaneous	6	7
Total	86	41

Table II shows a decided diminution in all of the important complications except postoperative hemorrhage. The seven miscellaneous conditions encountered only in series B were all of trivial importance, none of them jeopardizing life.

TABLE III.—GASTRO-INTESTINAL COMPLICATIONS

	Series A	Series B
Fecal fistula	6	6
Acute peritonitis	3	4
Acute intestinal obstruction	3	2
Pseudo-ileus	2	0
Paralytic ileus	1	1
Duodenal fistula		0
Acute dilatation of stomach		2
Acute parotitis	1	0
Total	16	6

It is a source of satisfaction to record the avoidance of all postoperative fistulas and organic intestinal obstructions. This may be fairly ascribed to the utmost gentleness in separating bowel adhesions, recognition of endometriosis of the rectovaginal septum during operation, refusal to irradiate any patient suspected of harboring a latent pelvic infection and careful peritonealization of all raw surfaces. In those instances in which a denuded surface oozed slightly or could not be satisfactorily covered otherwise, I have used sheets of gutta-percha tissue to prevent visceral agglutination, bringing the ends out through the lower angle of the abdominal wound.

Acute peritonitis supervened once within 24 hours after a radium application to a freely movable cervical stump for carcinoma, in another patient after a laparotomy for extensive papillary cystadenocarcinoma of the ovary in an elderly debilitated woman, in another case soon after a laparotomy for ruptured pyosalpinx and in a fourth patient after a celiotomy for retroversion, extensive pelvic adhesions, chronic appendicitis, and a dilated cecum. The three latter patients died.

The single instance of ileus was an incidental autopsy finding in the septic patient who had the ruptured pyosalpinx before operation and who really died of septicemia.

Acute dilatation of the stomach is no longer a postoperative sequel of consequence, since the Levine tube is now almost universally employed early to relieve gastric distress.

Red, spongy gums, or other evidence of pyorrhea, are deemed indications for postponing operation in all elective cases. Acute parotitis, always distressing, and often fatal, occurs not when mouth and teeth are clean.

In series A, 8 gastro-intestinal complications were regarded as preventable In series B, all 6 were apparently inevitable.

TABLE IV —PULMONARY COMPLICATIONS

	Series A	Series B
Pneumonia	12	1
Acute pulmonary edema	2	0
Pleurisy	1	1
Empyema	1	0
Pulmonary infarcts	1	2
Atelectasis	0	1
Bronchitis	0	5
Total	17	10

Although the difference in the incidence of pulmonary complications is gratifying, the most significant decrease is in the number of pneumonias In series A, there were 7 bronchial, 3 lobar, 1 influenza, and 1 hypostatic While this series of cases was accumulating, my ward patients were furnished anesthesia by comparatively inexperienced anesthetists In commenting in the previous paper on the fact that 11 of the 17 complications were noted in ward patients, I stated that "it seems fair to infer that the training of a larger number of anesthetists involves the risk of an increased number of pulmonary complications " The New York Post-Graduate Hospital soon thereafter abolished its course in anesthesia and practically all of the patients in series B were attended by skilled anesthetists However, I believe that another precautionary measure probably should be credited with the reduction in pulmonary complications in general, and the pneumonias in particular Coincidentally with the start of series B, I requested my anesthetists routinely to rebreathe every patient with 10 per cent carbon dioxide in oxygen just before the completion of the operation, irrespective of the anesthetic agent employed And in every case in which a patient manifested an excess of bronchial mucus or a tendency to cough, my resident carried out the same procedure two or three times daily until the danger signals disappeared The stimulation of the respiratory center as expressed by the prompt increase in respiratory rate, the depth of inspiration, and the pink tinging of the skin, as a result of the pulmonary hyperventilation, is so striking that I am convinced of its value, despite the pessimism of several experimental observers It seems logical to suspect that the 5 cases of bronchitis would have eventuated in bronchopneumonia without the protection of the carbon dioxide-oxygen administration

A succession of pulmonary infarcts, diagnosed by an internist, prolonged the convalescence in 2 cases, once after a vaginal plastic operation, and once after a hysterectomy for fibroids under spinal anesthesia

The single instance of atelectasis was a terminal massive collapse of the lungs discovered at autopsy in a patient dying of purulent peritonitis

There were no pulmonary complications in series B that can be regarded as having been preventable, and none that caused death

TABLE V —WOUND COMPLICATIONS

	Series A	Series B
Infected abdominal wounds	13	4
Dehiscence of abdominal wound	0	3
Hernia in abdominal wound	0	1
Hematoma of abdominal wound	0	1
Abdominal wound sinus	0	1
Infected perineal wounds	3	1
Hematoma of vulva	0	1
Total	16	12

Whereas the number of infections in primarily clean wounds is extremely low, the occurrence of disruption of the abdominal wound in 3 cases is not pleasant to contemplate One of these patients was markedly asthenic and developed a bronchitis with a racking cough 24 hours after a hysterectomy for fibroid On the sixth day she complained of pain in the region of the wound, with the issuance of a little blood tinged exudate between the sutures, and began to vomit Although the skin margins had apparently united, when the stitches were cut, two loops of gut were found insinuated between the peritoneal and fascial edges Another patient manifested the same symptoms on the eighth day, with a similar wound rupture The third patient was operated on under spinal anesthesia for multiple pathological conditions, and developed a dehiscence on the sixth day All three wounds were reopened under local anesthesia and resutured with through and through silkworm gut sutures after the eviscerated loops were replaced. The wounds

healed firmly thereafter In none of the wounds was there any trace of the catgut used for closure of the peritoneum and fascia. There must have been rapid proteolytic digestion of the catgut before fibroplastic production was sufficient to splint the wounds. The first two patients recovered the third died on the eighteenth postoperative day from peritonitis, pulmonary atelectasis, and fatty liver infiltration.

One patient presented a small hernia in the abdominal wound before her discharge from the hospital, probably caused by forcible vomiting early in her convalescence.

A small abdominal sinus persisted for a year after a fixation of the vagina to the abdominal wall, with reefing of the broad and round ligaments, for a post-hysterectomy prolapse. It closed after discharging a linen suture.

Approximation of the vaginal fibers of the levator ani muscles with kangaroo tendon and a subcuticular closure of the skin margins evidently minimize perineal wound infections, only one occurring in 218 perineorrhaphies in series B One hematoma of the vulva appeared 24 hours after the extirpation of a Bartholin cyst, probably because a small vessel that should have been ligated was overlooked.

The number of wound complications that might have been prevented is problematical

TABLE VI.—URINARY COMPLICATIONS

	Series A	Series B
Acute cystitis	5	4
Acute pyelitis	3	3
Suprapubic urinary fistula	1	0
Vesicovaginal fistula	0	1
Transitory hematuria	0	1
Total	11	9

Omitting cases of postoperative simple bladder irritation without acute inflammatory changes in the vesical wall, the incidence of cystitis was low in both series. This may be credited to routine catheterization every 6 hours for 3 days, irrespective of the inclination to void in hysterectomy cases and all others in which the bladder was subjected to trauma during operation Keeping the bladder free from overdistention precludes pressure on the suture lines after vaginal plastic operations and insures the absence of residual urine. I have no fear of an aseptic catheterization exciting a cystitis, but regard residual urine as a potential source of infection. When the patient voids for the first time, it is wise to catheterize immediately afterward for residual urine. If more than 20 cubic centimeters are recovered, the catheterization is repeated after each micturition until spontaneous evacuation is complete. Hexamethylenamine and acid sodium phosphate are prescribed early for all catheterized patients.

The incidence of postoperative pyelitis was lessened by pre-operative attention to bacteriuria and colonic stasis.

The vesicovaginal fistula developed in an extremely anemic woman who was given two blood transfusions before a panhysterectomy for fibroids, adenomyosis, and a diseased cervix. Urine leaked from a pin point opening in the vaginal cicatrix on the eighth postoperative day although voiding was not interrupted. The fistula closed spontaneously on the thirty-second day and was undoubtedly due to a small area of thrombosis in the bladder wall with subsequent necrosis.

Transitory hematuria appeared within 24 hours after a panhysterectomy and cleared up 48 hours later There was no evidence of a renal lesion.

In series A 9 urinary complications were regarded as preventable in series B, only 3.

TABLE VII.—CARDIOVASCULAR COMPLICATIONS

	Series A	Series B
Thrombophlebitis	4	6
Embolism	3	0
Tachycardia	1	1
Acute cardiac dilatation	1	0
Auricular fibrillation	1	0
Endocarditis	0	1
Total	11	8

Thrombophlebitis followed vaginal operations twice abdominal twice, and combined twice The pelvic veins were involved once, the left leg three times, the right leg once, and both legs once.

Although embolism occurred but three times in series A It did not occur at all in series B Perhaps this was due only to extraordinary good fortune but the practice of active motion of the extremities during con-

valescence, as well as the postponement of operation in elective cases until the cardiovascular system is in the best possible condition, cannot be ignored as contributing factors There were 179 abdominal hysterectomies in series A and 279 in series B, a total of 458, with only 1 death from embolism They were all done rapidly with clamps, which certainly refutes the argument that it is necessary to putter with ligatures before the uterus is removed for fear of possible embolism

Tachycardia was noted in 2 patients who were free from hyperthyroidism and organic heart disease, coming on within the first 24 postoperative hours It persisted for 5 days in 1, and 3 days in the other

Endocarditis was revealed at autopsy in a profoundly septic patient

None of these cardiovascular complications seems to have been preventable

TABLE VIII —SYSTEMIC COMPLICATIONS

	Series A	Series B
Surgical shock	2	2
Acidosis	2	1
Uremia	1	0
Alkalosis	1	0
Thyrotoxicosis	1	1
Total	7	4

Surgical shock can be greatly restricted by the free use of pre-operative blood transfusions Transfusions are given to all patients on my service with a red cell count of 3,500,000 or less, or hemoglobin of 60 per cent or less, and all septic or debilitated women They were so used in 35 patients in series B The 2 cases of shock in series A occurred in septic patients, the 2 in series B developed after prolonged, and technically difficult laparotomies

The patient in series B who developed acidosis was an advanced diabetic with a hopeless carcinoma of the cervix, who died 10 days after admission She really should have died on the medical service I have a great many diabetic candidates for operation, and usually have no difficulty in converting them into favorable prospects by rest in bed, dietary restrictions, and the use of insulin

Thyrotoxicosis occurred in a patient after curettage who had been referred by the surgical department for therapeutic abortion because of hyperthyroidism

I know of no way in which these systemic complications could have been prevented

TABLE IX —POSTOPERATIVE HEMORRHAGE

	Series A	Series B
Postoperative hemorrhage	3	4

A postoperative hemorrhage is always humiliating In series B the first consisted of bleeding from the abdominal wound 24 hours after operation, and must have been due to stabbing a superficial vessel in closing the skin The second arose from the cervical stump 8 days after a supravaginal hysterectomy in a luetic patient, and was probably due to necrobiosis The third came from the cervical stump 6 days after a Schroeder amputation, despite the use of 40 day chromic catgut The fourth consisted of oozing on the eighth day from the suture line over an anterior colporrhaphy They were all easily controlled, three of them were preventable

TABLE X —MISCELLANEOUS COMPLICATIONS

	Series A	Series B
Parametritis	0	3
Abscess of thigh	0	1
"Ether eye"	0	1
Postoperative psychosis	0	1
Abscess of nasal septum	0	1
Total	0	7

A unilateral parametritis followed a hysterectomy and salpingo-oophorectomy for fibroids in 3 cases, in all of which it was necessary to invade the cellular connective tissue of the parametrium to enucleate tumors The parametritis was recognized promptly and in all it cleared up under treatment before the suppurative stage

An abscess of the thigh developed following a hypodermoclysis of glucose, given by the resident because the patient was in mild shock, and he could not penetrate a vein There is now a standing order that nothing but normal saline solution or Ringer's solution shall be given by hypodermoclysis

One patient suffered from acute conjunctivitis of one eye immediately after reacting from the anesthesia This was certainly the fault of the anesthetist, and not that of the operator

TABLE XI—MORTALITY IN ONE THOUSAND CONSECUTIVE GYNECOLOGICAL OPERATIONS

No.	Diagnosis	Operation	Cause of death
1	Secondary anemia, fibromyoma of uterus, pelvic adhesions	Transfusion of pint [illegible] of blood [illegible] and bilateral salpingo-oophorectomy (gas-oxygen anesthesia)	Simultaneous cessation of respiration and heart beat on the [illegible] table, [illegible] minutes after the operation was started. No autopsy. (Anesthetic death)
	Diabetes, destruction of pancreas after [illegible] by another operator, advanced tuberculosis of cervix	Autopsy (gas-oxygen anesthesia)	Diabetic acidosis, 10th day
3	Carcinoma of liver	Exploratory laparotomy (limited opens by [illegible]), evacuation of ascites fluid (gas-oxygen anesthesia)	Esophageal hemorrhage, cirrhosis of liver, 6th day. Autopsy
	Tubal pregnancy	Right salpingectomy (gas-oxygen-ether anesthesia)	Two [illegible] on 8th day after [illegible]. Death [illegible] later. Uniform renal degeneration. Autopsy
5	Extended pneumonia, pelvic adhesions, retroversion of uterus, chronic appendicitis, [illegible] of ovarian	Permanently [illegible] of uterus, [illegible] of uterus, appendicectomy, [illegible] of ovarian (spinal anesthesia)	Wound dehiscence, 8th day. Wound [illegible] under local anesthesia. Died 17th day. Lobular pneumonia, [illegible], [illegible] infection, fatty liver degeneration. Autopsy
6	Degenerated uterine fibroid, pelvic abscess, septicemia	Vaginal [illegible] (posterior colpotomy followed by blood transfusion) (gas-oxygen anesthesia)	Died 5th day. Ruptured appendix, [illegible], septicemia, endocarditis. Autopsy
7	Adenocarcinoma of ovary, ascites	Pre-operative transfusion, bilateral salpingo-oophorectomy (gas-oxygen-ether anesthesia)	Pneumonia. Death on 6th day
8	Fibromyoma of uterus, ovarian cyst, chronic appendicitis	Supravaginal hysterectomy, right salpingo-oophorectomy, appendicectomy (gas-oxygen-ether anesthesia)	Post-operative shock in 6 hours. Transfusion. Died 14 hours. Bilateral hemorrhage. Autopsy

One patient operated on for bilateral papillary cystadenocarcinoma of the ovary developed a transitory psychosis on the sixth day which cleared up within a month

An abscess of the nasal septum can hardly be considered a true postoperative complication after a laparotomy but in one case it was responsible for an obscure postoperative pyrexia, which subsided after drainage of the pyogenic focus.

MORTALITY

The first case was a death during operation called an "anesthetic death" by the expert anesthetist who administered the ether and may be regarded as one of the accidents of surgery

The second and third patients were in a desperate condition and really belonged on the medical service Neither operation was approached with any enthusiasm

The fourth death was inexplicable, as the autopsy failed to reveal the cause of the convulsions and the renal degeneration was a microscopical diagnosis

In the fifth case the spinal anesthesia was unsatisfactory and had to be supplemented with nitrous oxide gas-oxygen The obese patient retched and strained throughout the primary operation. Perhaps this was a factor in the subsequent wound disruption. Spinal anesthesia was used 72 times in this series of 1000 cases, and in only 3 was the relaxation unsatisfactory

The sixth patient was too sick on admission to justify a laparotomy and when her hyperpyrexia was unaffected by the posterior colpotomy and pelvic drainage, the prognosis became grave indeed

The seventh patient was a debilitated elderly woman whose abdomen was so distended by the tumors and fluid that dyspnea was marked. She demanded relief realizing the risks involved.

The eighth death was due to my personal obstinacy At 4 p m after operation the patient's pulse rate was 90, and remained so until 8 p m. The rate then increased and reached 120 within an hour A glucose infusion was given at 10 p m. and a blood transfusion at 12 midnight. There was no restlessness or air hunger and I could not believe that she was bleeding internally because I always secure the ovarian and uterine vessels with transfixion ligation, and assure myself that the field is absolutely dry before closing

the abdomen The autopsy revealed an internal hemorrhage apparently arising from the right side of the top of the cervical stump beneath the area covered by the bladder Histological examination of the cervical stump showed that the uterine artery and vein were firmly encircled and compressed by the ligature

In series A, 5 of the 19 deaths were regarded as preventable In series B only 1, the eighth, can be so designated

CONCLUSIONS

1 Having conscientiously scrutinized a previous series of 1000 consecutive personal gynecological operative cases, it has been possible to effect a 34 per cent reduction in morbidity and a 57 per cent reduction in mortality In the second series of 1000 there was morbidity in 53 patients and 8 patients died

2 Gentleness in separating bowel adhesions, recognition of endometriosis of the rectovaginal septum, refusal to irradiate any patient suspected of harboring a latent pelvic infection, careful peritonealization of raw surfaces, and the use of sheets of gutta-percha tissue to cover surfaces that cannot be peritonealized will obviate fecal fistulas and postoperative intestinal obstruction

3 The routine administration of 10 per cent carbon dioxide in oxygen just before the completion of the operation will minimize the incidence of pulmonary complications in general, and pneumonia in particular

4 Dehiscence of an abdominal wound is probably due to tissue hunger and proteolytic digestion of catgut before fibro-plastic production is sufficient to splint the wound rather than to defective suture material

5 Approximation of the vaginal fibers of the levator ani muscles with kangaroo tendon and a subcuticular suture of the skin margin evidently minimize perineal wound infections

6 Keeping the bladder free from residual urine lessens the incidence of postoperative cystitis Residual urine is more of a menace than aseptic catheterization

7 Postponing elective operations until the cardiovascular system is in the best possible condition and the frequent practice of active motion of the extremities throughout convalescence will practically eliminate postoperative embolism

8 Removing the uterus by applying clamps instead of preliminary ligatures is a safe procedure

9 Pre-operative blood transfusions should be utilized in all cases of anemia, debility, or sepsis

10 Invasion of the cellular connective tissue of the parametrium for the removal of intraligamentary tumors predisposes to subsequent parametritis

11 Glucose should always be administered intravenously, never subcutaneously

12 It should be the aim of every pelvic surgeon to limit his postoperative morbidity and mortality to an irreducible minimum

ROENTGEN PELVIMETRY AND FETAL CEPHALOMETRY

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IN the care of an obstetrical patient it is important to establish a *fetal head-pelvic diameter ratio* Many methods have been described by which this ratio might be ascertained. Probably the one most often used is some modification of a digital examination with the aid of calipers or a rule. Even though it were possible to measure the cardinal diameters of the pelvis, the difficulties in measuring the fetal head are too great to overcome except by roentgenographic methods

This article presents a previously described technique of pelvimetry and fetal cephalometry by which there is a comparison between the *volume* of the fetal cranium and the *volume capacity* of two pelvic *diameters*—the true conjugate and the ischial spine. Also it includes roentgenographic studies on the absolute rate of increase in volume of the fetal cranium *in utero*

The fetal cranium in utero is a spheroid object and if the circumference of a spheroid is measured at any two right angle planes the mean measurement can be used to calculate the volume. The volume of a sphere as proved by geometry equals the area of the surface times one third of the radius or stated as a formula

$$V = \frac{1}{3}S = \frac{1}{3}\pi R^3 = \frac{1}{6}\pi D^3 = 0.5236 D^3$$

Therefore, it is simple arithmetic to calculate the volume of the fetal cranium from the mean circumference measurement The unit of volume, the liter, is used to express the size

In the human female pelvis except in the *funnel type the anteroposterior (true conjugate)* or the ischial spine is always the smallest (Within the limits of the author's investigation this has been found to be true) If these two diameters are measured, it is easy to calculate the volume of a sphere which could be placed in a space of that size This can be expressed as the volume capacity of the diameter When the fetal cranium and pelvic diameters have been measured in units of volume and volume capacity respectively a definite *fetal cranium-pelvic diameter ratio is evolved*

The mechanism of labor includes a hydrodynamic problem. It may be thought of as a mass of a certain volume which has to pass through an opening of a known volume capacity Molding of the fetal cranium is the result of a shift in volume of a spheroid as it is forced through an opening of smaller volume capacity Thus it is valuable information to *determine the amount of shift in volume* (molding) that may occur without a fetal mortality When the *fetal cranium—smallest pelvic diameter ratio* is established antepartum, the probability of a fetal mortality can be reckoned

It is advantageous to determine this ratio before the onset of labor It can be done 5 to 10 weeks before term from the graph in Figure 1 which shows the rate of increase in *volume of the cranial skull in utero* and the size at any subsequent time. It will facilitate the use of this graph to trace the curve on cellophane and shift the curve up or down to correspond with the size of cranium and estimated weeks of gestation

This curve, Figure 1 was plotted from serial roentgenograms during gestation. It may show racial variation, but in this locality Chattanooga, there was no marked difference between the *white and negro* It has been reliable to within less than 10 per cent error in cases examined 10 weeks *before term* Figure 2 shows a lateral roentgenograph of a primipara negro, examined at the thirty *sixth week of gestation*. The true conjugate was smaller than the ischial spine diameter The ratio revealed a *fetal cranium 100 milliliters* (cubic centimeter) greater than the volume capacity of the smallest pelvic diameter Four weeks later the patient was re-examined and had an increase in volume of 80 milliliters during this time (Fig 3) The disproportion is obvious After 54 hours of labor she delivered a live baby which showed extreme molding Other cases with a similar

term were not so fortunate There
ı an 80 per cent fetal mortality rate
ases with unengaged heads which
a fetal cranial volume of 150 milli-
eater than the volume capacity of the
jugate diameter The bischial spine
r volume capacity may permit a
variation in ratio but that depends
e type pelvis which will be discussed
this article

, technique of the roentgenographic
tion of the pregnant woman for men-
, I measure three variable factors,
n circumference of the fetal cranial
---, the true conjugate and the bischial spine diameters The mean *perimeter measurement* has the advantage of no interference due to oblique positions of the fetal skull The two diameters of the pelvis must be parallel to the film when they are exposed to prevent elongation or foreshortening of the film image With the patient supine, the bischial spine diameter is parallel Likewise, in the true lateral recumbent position, the true conjugate diameter lies parallel to the film From these two exposures, all the measurements are made when the fetus is in cephalic presentation In breech cases, an additional anteroposterior and lateral roentgenograph is made with the central ray passing through the fetal head About 95 per cent of cases will be in cephalic presentation The film image magnification is corrected by the use of a calculator later described

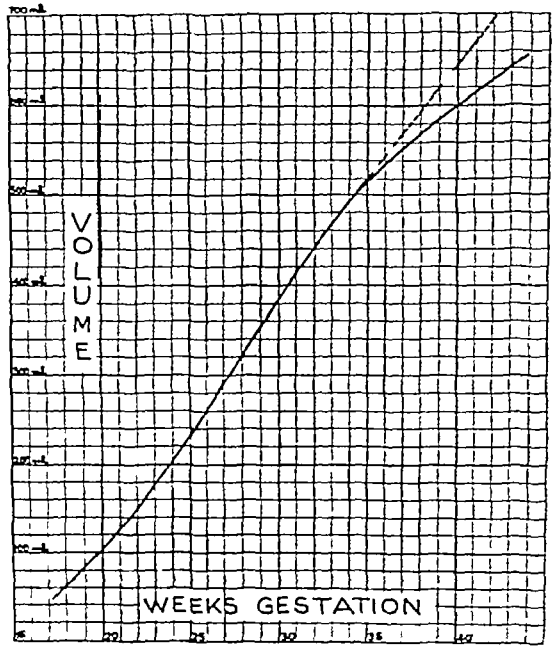


Fig 1 Graph showing absolute rate of increase in volume of the fetal head *in utero*

ROENTGENOGRAPHIC TECHNIQUE

The patient is placed supine with the median plane over the center line of the Potter-Bucky diaphragm The central ray is pro-

Fig 2 Lateral roentgenogram of primipara aged 17 at 36 weeks' gestation

Fig 3 Same patient as shown in Figure 2, in labor at the fortieth week of gestation

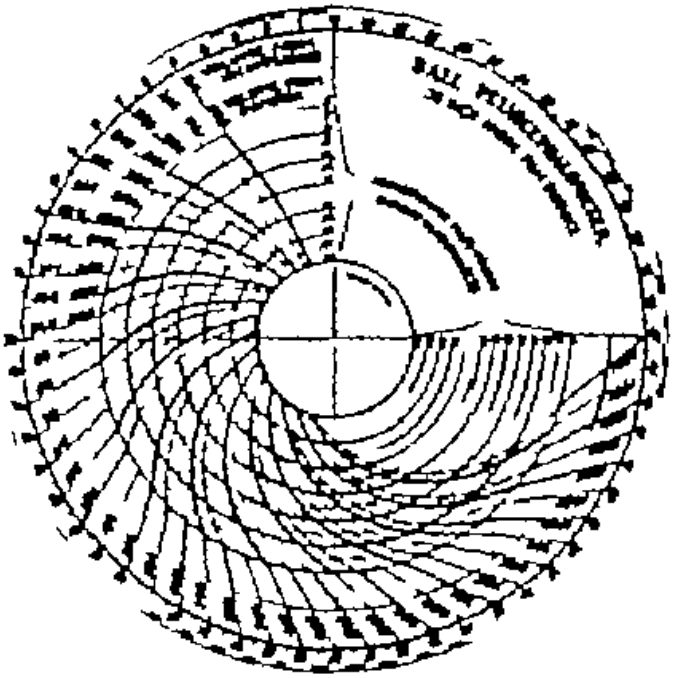


Fig. 4. A calculator for correcting roentgenographic magnification without mathematical computation.

jected vertically through a point midway between the antero-inferior iliac spines. The anode-film distance should correspond to that which is marked on the calculator (Fig. 4, 30 inches). A 14 by 17 inch film is placed transversely to the pelvis to include the greater trochanters. A single exposure is made which requires about 80 kilovolts and 100 milliampere seconds.

In each instance, a "Left" or "Right" lead marker is placed *on the cassette*. It is not necessary to measure the patient or to place any markers on her to localize anatomical points used in the computation. In cases of breech presentation or multiple pregnancy additional roentgenographs must be made to include the fetal skull at right angle views. For these additional roentgenographs, the central ray should pass about 5 centimeters below the inferior margin of the tip of the xiphoid process of the sternum, in the antero-posterior projection and in the true lateral projection, over the median plane of the body at the same level.

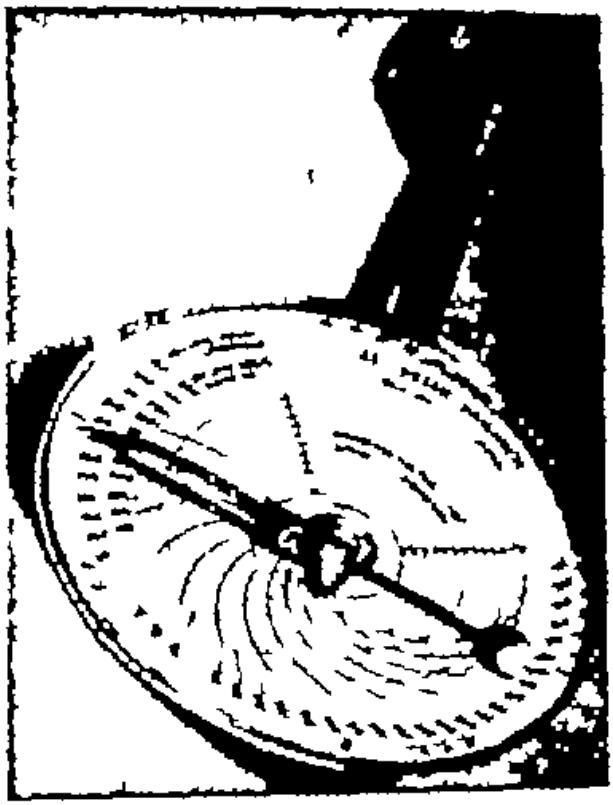


Fig. 6. The pelvicephalometer.

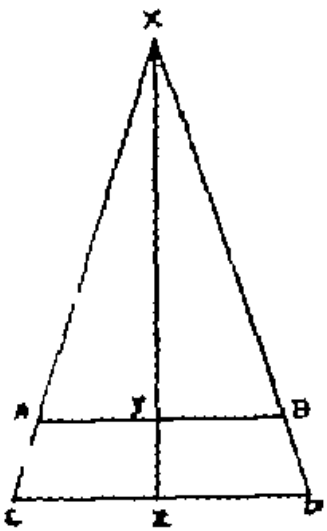


Fig. 5.

THE PELVICEPHALOMETER

When an X-ray exposure is made the roentgenographic image naturally shows a certain degree of enlargement depending upon the distances of the object from the film and from the anode. In the diagram, Figure 5, X represents the anode, AB the object, CD the film, XZ the anode film distance and XY the anode object distance. The object AB will be registered upon the film as size CD if the object film distance is YZ and the anode film distance is XZ or CD/AB = XZ/XY. If one of the three variable factors—anode film distance, XZ—is made constant a correction chart for the other two YZ and CD can be

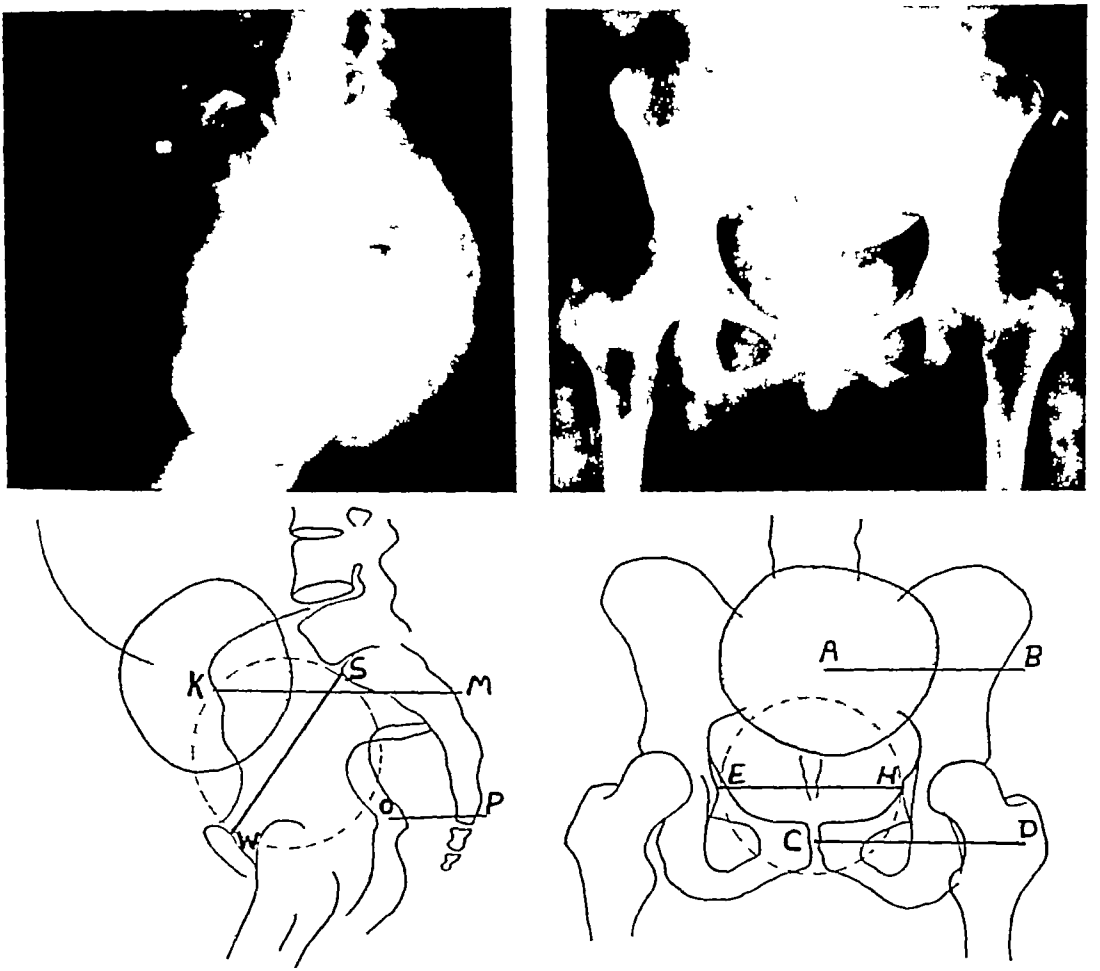


Fig 7 Anteroposterior and lateral roentgenograms of a near term pregnant woman with fetus in cephalic presentation left occipito-anterior position The outline of the roentgenographic anatomy is used to illustrate the method of computing *fetal cranium—smallest pelvic diameter ratio*

plotted with rectangular or polar co-ordinates (Fig 4)

In this method, a 25 inch, 30 inch, or 36 inch anode film distance is arbitrarily selected and the 2 other variables are corrected by means of the pelvicephalometer (Fig 6) This instrument consists of a calculator (dial) to which is attached a pointer, *A*, connected to the rotor, *B*, by a shaft and gear so that the pointer always indicates the distance traveled by the rotor, i e , the size of the roentgenographic image

The calculator (Fig 4) is a circular rule obtained by the plotting of polar co-ordinates —the points being located arbitrarily There are 60 centimeter divisions on the perimeter of the calculator, and the subjacent radial curved lines are intersected by concentric circles which represent the *object film* distances in centimeters

The two tables on the calculator represent in milliliters the volume of a sphere of a known circumference or diameter These tables are used to compare the volume of the fetal head with the volume capacity of a pelvic diameter By this means the passenger passage ratio can be expressed in similar units, and the amount of molding necessary for the

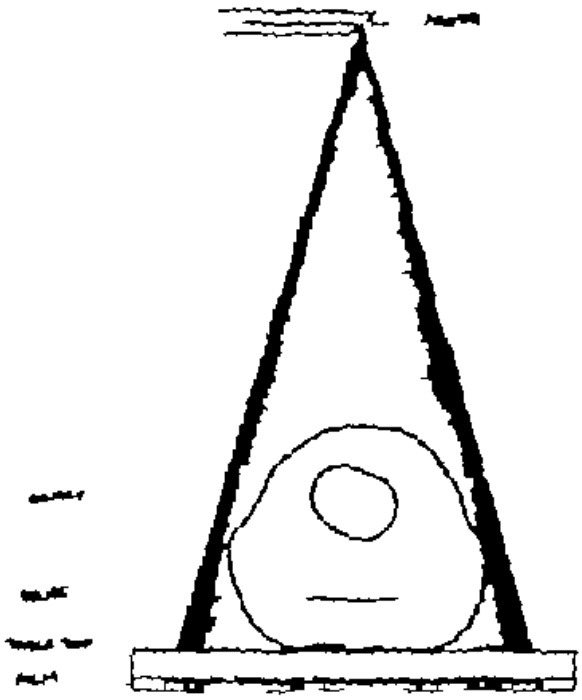


Fig 8 A drawing illustrating roentgenographic magnification

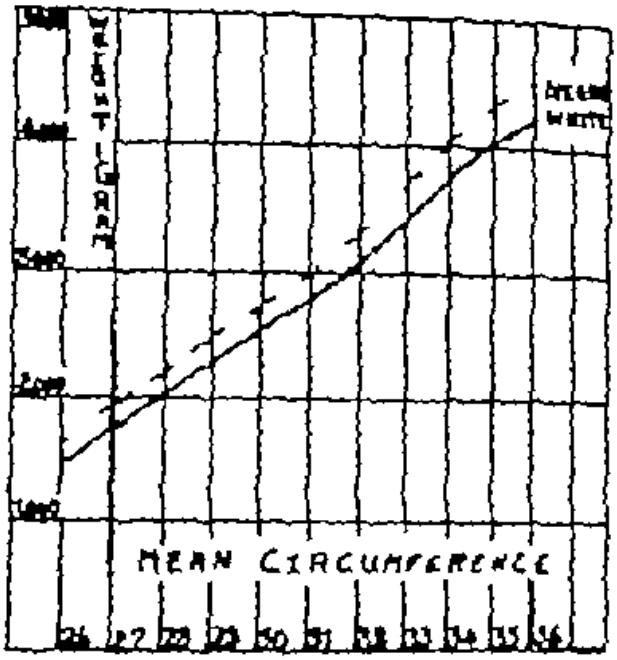


Fig 9 A graph showing average weight of newborn in relation to the mean circumference in centimeters of the fetal cranium

head to pass through the pelvic diameter can be better *visualized*

When the roentgenographic image is measured and the object film distance is known the pointer is retraced—by manipulating the rotor with the finger over the radial line subjacent to the centimeter size until it rests over the point of intersection of the concentric circle and the subjacent line Figures corresponding to the concentric circles appear on the pointer for convenience in locating the point of intersection After the pointer is placed at the intersection the corrected size is read from the figure in the outer row over which rests the tip of the pointer Hence by the use of this instrument a linear or spheroid roentgenographic image can be measured and its magnification corrected simply by shifting the pointer of the pelvicephalometer The determination of object film distance is described in the method of computation

METHOD OF COMPUTATION

The anteroposterior and lateral roentgenographs are placed before illuminators and the usual observations regarding abnormalities, presentation of the fetus type of pelvis degree of engagement of fetal head etc noted The circumference of the fetal skull as shown in the anteroposterior roentgenogram (Fig 7) is measured by tracing the perimeter of the image as outlined The pointer on the pelvicephalometer is set at zero and the rotor traced around the periphery of the skull image in a counterclockwise direction The distance from the fetal skull to the table top in the anteroposterior direction is determined by measuring, on the lateral roentgenograph (Fig 7) the distance in centimeters from the center of the fetal head to the spine of the sacrum (*K M* Fig 7) the line of measurement being the path of central ray when the anteroposterior roentgenograph was exposed The distance from the table top to the film (Fig 8) then must be added to determine the total distance from the fetal head to the film

The points *A B C D K M* and *O-P* in Figure 7 were arbitrarily selected after many patients were examined by external measurements and compared with roentgenographic images of the pelvis It was found that the thickness of the soft tissue was about equal to the increase in size of the bone image on the roentgenogram (usual magnification) Therefore the distances *A B C D K M* and *O-P* in Figure 7 were found to be accurate enough for clinical purposes to determine the distance of the object from the film when the table top is

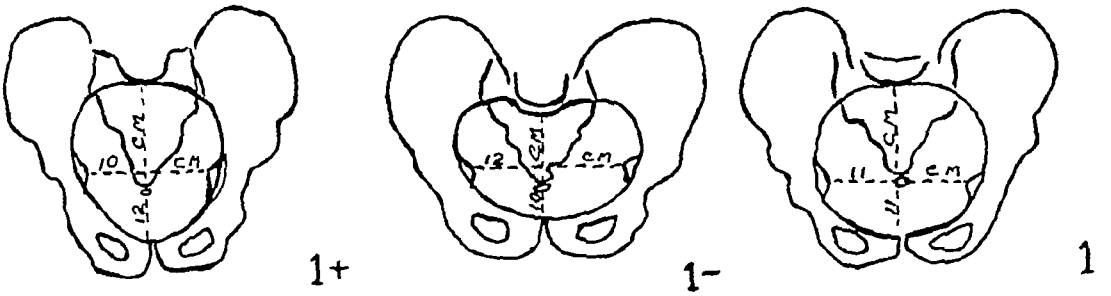


Fig 10 Schematic drawing of types of pelves classified by measuring the true conjugate and ischial spine diameters

film distance was added to this measurement

The two measurements of the perimeter of the fetal skull represent the circumferences of a spheroid, from them the mean circumference must be determined to calculate the volume of a sphere After this circumference has been determined, 2 centimeters are added to allow for the soft tissues of the scalp, which allowance has been found to be the average scalp thickness The volume of the fetal head then is read from the outer table on the calculator —*volume from circumference*

Two pelvic diameters then are determined The anteroposterior—true conjugate—is measured on the lateral roentgenogram, *W-S* in Figure 7, by tracing the rotor of the pelvicephalometer in a straight line from the anterosuperior border of the promontory of the sacrum to the posterior border of the symphysis pubis The posterior border of the symphysis pubis is recognized by the posterior cortex of the pubis The correction for the object film distance of this diameter is made by measuring on the anteroposterior roentgenogram the distance from the symphysis pubis to the plane of the midline of the greater trochanter, *C-D* in Figure 7 The correction is made on the calculator and the pelvic diameter is read The other pelvic diameter, measured in a similar manner, is the ischial spine diameter, *E-H* in Figure 7 The object film distance of this plane is determined from the lateral roentgenogram by measuring from the ischial spine to the posterior border of the coccyx or lower sacrum, *O-P* in Figure 7 The linear magnification then is corrected by the use of the calculator

The volume capacity of the pelvic diameter then is translated into a sphere of this diameter by reading the inner table on the calculator—*volume from diameter* The broken circles in Figure 7, graphically represent the midplane of this sphere

WEIGHT OF FETUS IN UTERO

The estimate of the weight of the fetus *in utero* is a simple matter of reference to a chart showing the average weight of the newborn compared to the mean circumference of the head (Fig 9) There are variations due to sex, race, parity, and disease which make considerable difference between the estimated and actual weight In normal average cases, the chart is fairly reliable However, it is the size of the cranial skull, rather than total body weight, that is important in the mechanism of labor

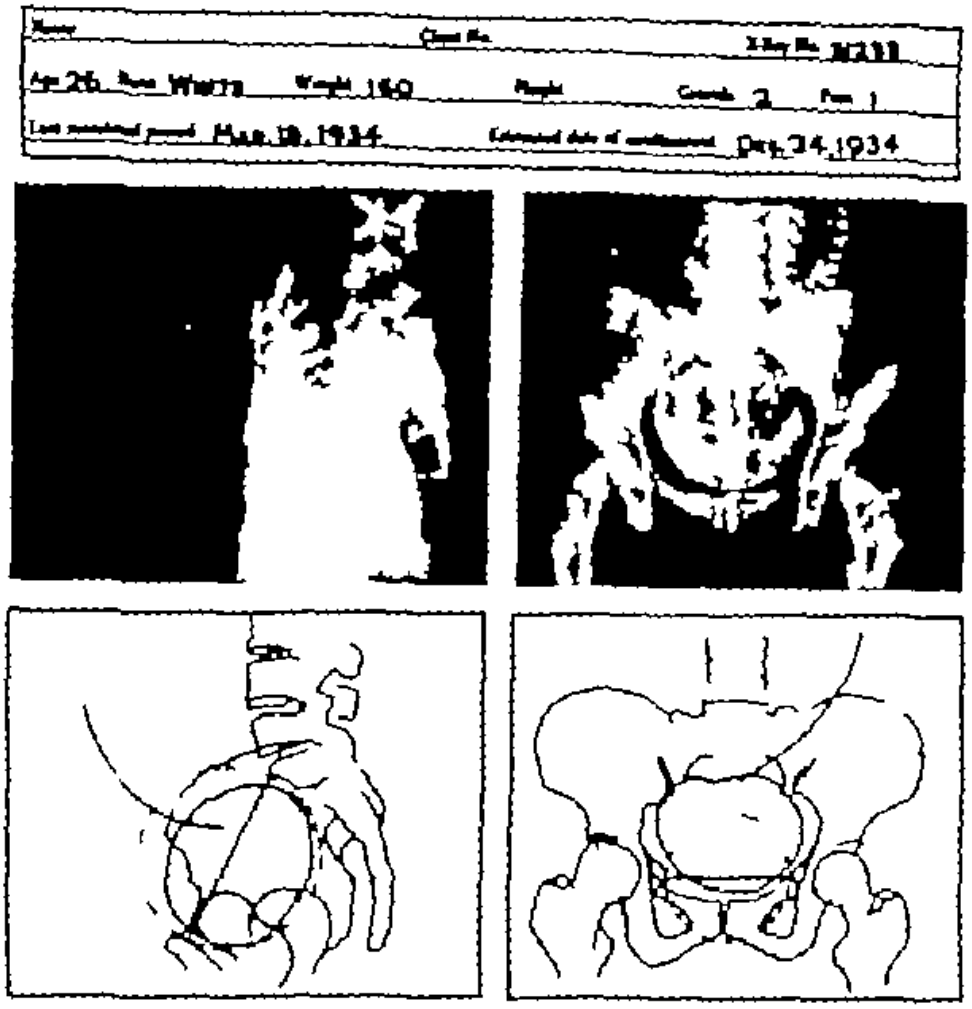
As an aid in determining the viability of premature infants on the basis of weight, Figure 9 will be of value

CLASSIFICATION OF PELVES

There are classifications of pelves based upon the size as a whole also including deformities with a descriptive adjective de-

TABLE 1 —INCIDENCE OF TYPE PELVES CLASSIFIED ACCORDING TO THE PELVIS INDEX SEE FIGURE 10

Type of pelvis	White		Negro		Total	Total
	Cases	Incidence per cent	Cases	Incidence per cent	Cases	Incidence per cent
Index one plus	56	40	14	22	70	35
Index one minus	32	20	18	30	50	25
Index one	50	40	30	48	80	40
Total	138		62		200	



ROENTGENOGRAPHIC EXAMINATION

Date	Presentation Position	Type of Pelvis	Conjugate			Pelvic Diameters		Pelvic Index	Fetal Head Diameter	Fetal Weight
			A.P.	Lat.	Trans.	A.P.	Transverse			
7-24-34	L O A.	1+	30.4	31.8	31	11.6	10.6	6.10	6.00	7 10

POSTPARTUM DATA BIRTH

Date	Presentation			Type Delivery	Fetal Position	Conjugate			Delivery	Sex	Weight
	Ant.	Lat.	Ant.			A.P.	Lat.	Trans.			
7-24-34	3	30'	10'	SPONT.	NORM	31	33	32	SVD	F	7-1

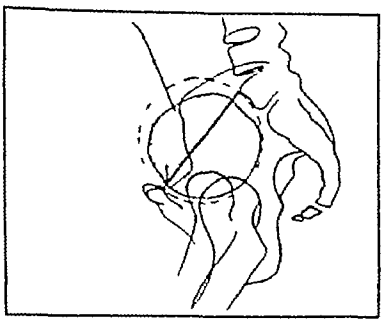
Fig

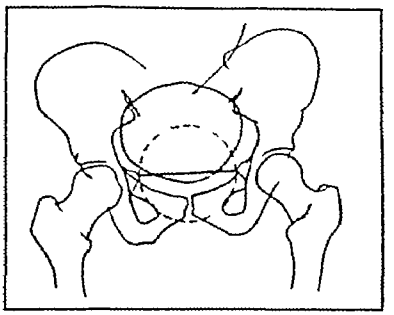
Figs 1 to 5 inclusive are illustrated case reports of different positions of the fetus They show the accuracy and reliability of the technique described

noting the etiology A recent excellent classification, based upon anthropological studies, has been published by Caldwell, Moloy and associates For the sake of clearness, it is desirable to use some classification in reporting the roentgenographic examination of the pelvis Since in the above described technique, there is a ratio established between two important pelvi diameters and the fetal head it has been found convenient to classify the pelvis from the diameter measurements

A pelvis index is obtained from the two diameter measurements by placing the true conjugate as the numerator and the biischial spine as the denominator of a fraction (Fig 10) An ovoid pelvis with the long diameter anteroposteriorly obviously has a pelvis index of one plus When the long diameter is trans-

Name		Chart No. 6271		X-Ray No. 31102	
Age 20	Race WHITE	Weight 138	Height 65	Gravida 2	Para 0
Last menstrual period MARCH 11, 1934			Estimated date of confinement DEC 1934		





ROENTGENOGRAPHIC EXAMINATION

Date	Presentation	Type of Pelvis	Circumference of Cranial Skull A. P.	Lat.	Mean	Pelvic Diameters A. P.	Ischial Spines	Vol. Cap. amniotic pel. dia.	Vol. of Head Plus Scalp	Approx. Weight
12/4/34	Pos LOT	1	29	272	281	97	98	460	460	5-12

POSTPARTUM DATA BIRTH

Date	Hours Labor 1st	2nd	3rd	Type of Delivery	Amount of Head Molding	Circumferences S. O. B.	O. F.	Mean	Volume	Sex	Weight
12/4/34	19	12	45'	SPONT	SLIGHT	30	31 5	30.7	480	F	5-11

Fig 12

versely the pelvis index is one minus When the two diameters are about equal or within 5 millimeters—measurable error—the pelvis index is one

It is interesting to note the difference in incidence of these types as they occurred in 200 consecutive cases, Table I, in both the white and negro The measurements of these two diameters from roentgenographic examination have not previously been reported in the literature as a series so that a comparison is not available However, it is a routine of many practitioners to measure these diameters, and from their figures it could be compared

By this simple classification, there is no definite idea of the volume capacity of the posterior pelvic outlet In some cases, the sciatic notch arch is wide and the sacrum has a deep concavity In these cases the biischial

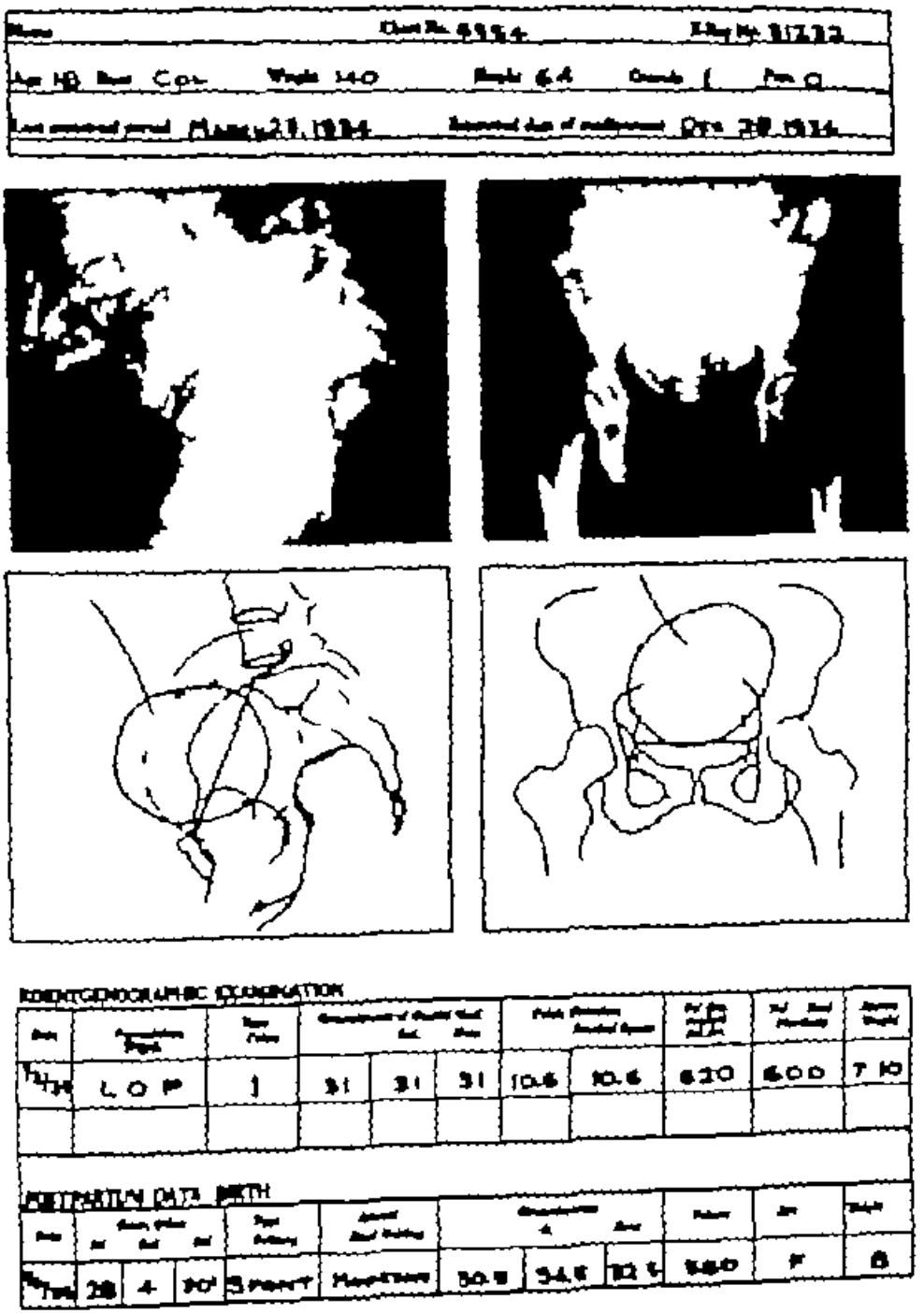
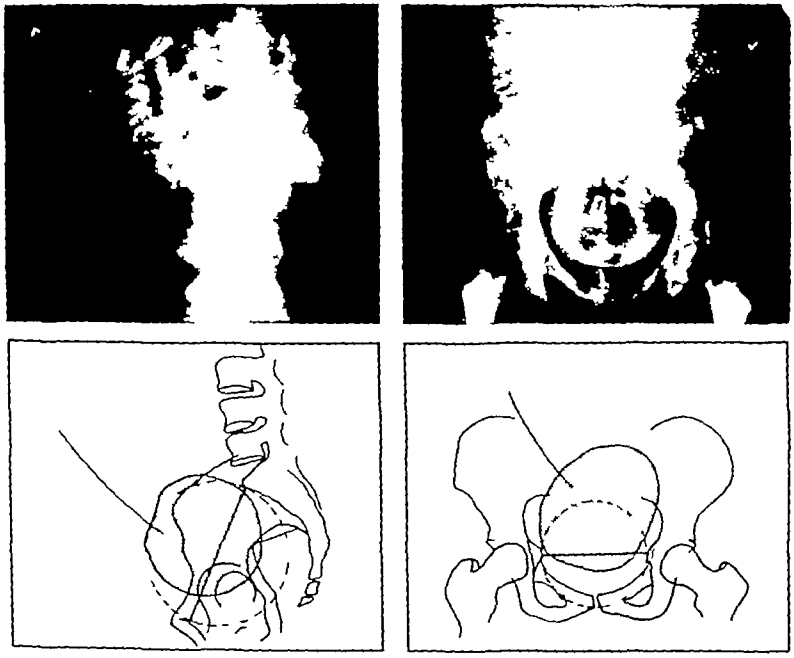


Fig. 13

spine diameter measurement may show a head diameter ratio which would indicate a disproportion but no difficulty would be encountered due to this very large volume capacity of the posterior pelvic outlet. In other cases, the sacrum may have very slight concavity and the sciatic notch arch be very narrow. It appears that the width and depth of the pubic arch are more important to determine the volume capacity of the outlet, while the sciatic arch is indicative of posterior pelvic capacity which permits rotation of the fetal head to the most favorable position to pass through the bifischial spine diameter. The bifischial spine diameter will determine whether rotation is necessary for spontaneous delivery by comparing its volume capacity with the volume of the fetal cranium. Anyhow the measurement from the film will state the minimum of volume capacity of this diameter.

Name	Chart No. 6682	X-Ray No. 31261
Age 16 Race WHITE Weight 145	Height 65" Gravida 1	Para 0
Last menstrual period MAR 16, 1934	Estimated date of confinement DEC 16, 1934	



ROENTGENOGRAPHIC EXAMINATION

Date	Presentation Pos	Type of Pelvis	Circumference of Cranial Shell A P	Lat	Mean	Pelvic Diameters A P	Bituchial Spines	Vol. Cap. emptied per div.	Vol. of Head Plus Scalp	Approx Weight
1/7/35	ROT		31-4	31-2	31-3	11-6	11-4	790	620	8-2

POSTPARTUM DATA BIRTH

Date	Hours Labor 1st	2nd	3rd	Type of Delivery	Amount of Head Molding	Circumference S. O. B.	O. F.	Mean	Volume	Sex	Weight
1/7/35	9	1	30'	SPONT	SLIGHT	31-5	34	32-7	580	F	7-8

Fig 14

a misinterpretation will be in patients favor

It will require a large series of cases to establish a fairly reliable index of disproportion in units of volume, and the series should be a compilation of different examiners to eliminate the personal equation so common in a work of this nature Of course it is appreciated that many factors must be taken into consideration in determining a normal margin of safety, but the cranial volume—pelvic diameter ratio is the most important factor

The accuracy of the technique described is illustrated in Figures 11 to 15, inclusive In general it may be said that there has been a maximum error of 10 per cent in volume and 5 per cent in linear diameter measurements

SUMMARY

A roentgenographic technique for determining the fetal cranium—pelvic diameter ratio

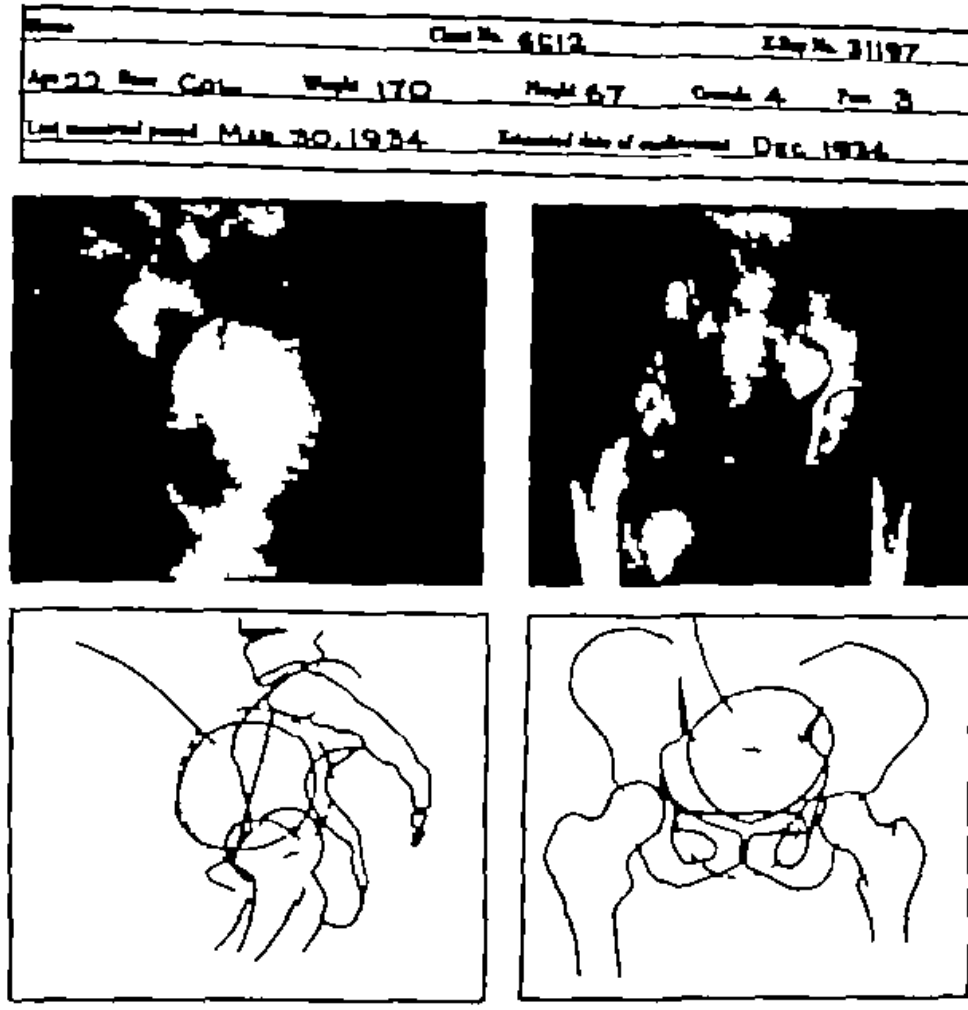


Fig 15

in units of volume is presented which requires only two films and does not involve any mathematical computation.

The absolute rate of increase in volume of the fetal cranium *in utero* as obtained from roentgenographic data is shown.

A new instrument the pelvicephalometer for correcting the magnification of a roentgenographic image and its application to obstetrical patients is described.

A simple classification of pelves from a roentgenographic examination is briefly discussed.

Several case reports are presented in a graphic form for comparison and to show the accuracy of the procedure.

I wish to express my appreciation of the valuable suggestions and encouragement given by Dr. Edward F Buckner J and the co-operation of the staffs of both the Barnards Erlanger and the Children's Hospitals

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Fig. Photograph of accessory biliary vesicle arising from hepatic duct. Small wooden pegs are shown projecting into the openings of tributary ducts.

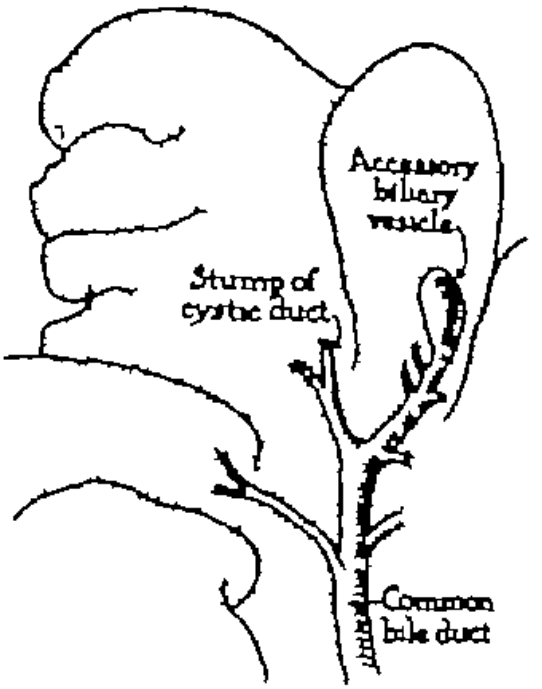


Fig. 2 Diagram showing anomalous ductular gall bladder arising from hepatic duct

accumulated inflammatory cells were polymorphonuclear leucocytes In other cases they were lymphocytes This is in agreement with the report of Troitsky who described the development of hepatitis and perihepatitis interstitialis chronica levis" following cholecystectomy

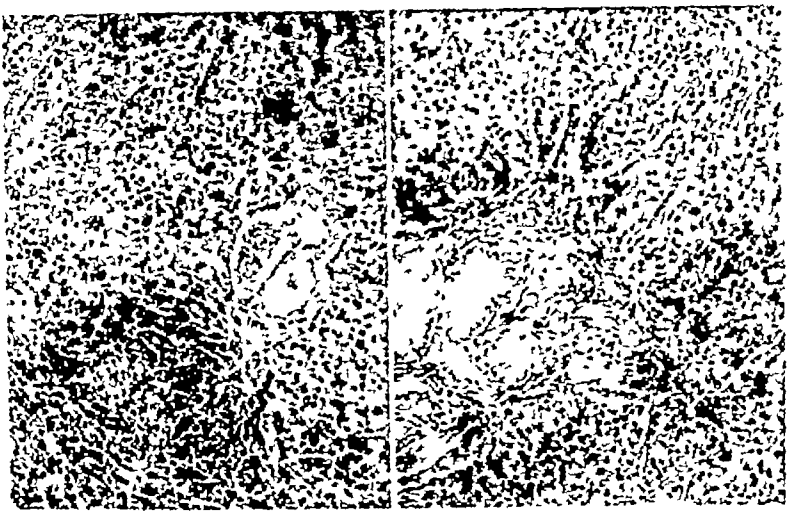
An incidental finding worthy of mention was a small accessory biliary vesicle 1 centimeter in diameter arising from an hepatic duct of dog 2 The anomalous ductular vesicle is shown in the accompanying photograph and drawing Boyden has pointed out that ductular gall bladders are not derived embryologically from the cystic diverticulum but from the hepatic duct itself In our experience such accessory vesicles are very uncommon in the dog

COMMENT

Following cholecystectomy there is often but not always a gross dilatation of the extrahepatic biliary ducts The dilatation however is much less than is observed in cases of mechanical obstruction (4) such as occur in the presence of stone, stricture or neoplasm, presumably because the intraductal pressure does not attain such a high level in the former as in the latter condition Potter and Mann reported that immediately after cholecystectomy there is a rise in the pressure within the common duct while Puestow found the intraductal pressure to be reduced Puestow's preparation however differed from that of Potter and Mann in that the common duct did not lead into the normal intestine but into the longitudinally slit duodenum brought to the outside of the animal's body

The cause of the increased intraductal pressure which leads to dilatation has generally been said to be resistance to the outflow of bile by the intramural sphincter mechanism (9 12 13 15 21) In the absence of the gall bladder which normally acts as a pressure regulator the increased pressure must be accommodated by dilatation of the duct Judd and Mann (13) reported that dilatation did not occur (except in 1 case) when the sphincter was cut, unless there was a mechanical obstruction due to scar formation

While it is probable that resistance at the sphincter is the cause of dilatation of the ducts



Figs 3 and 4 These two photomicrographs show the type of cellular reaction observed in the liver of the cholecystectomized dogs These changes were not present in the liver at the time the cholecystectomy was performed

in some instances, there are many cases in which such an explanation is inadequate Cox found that the dilatation begins very early following cholecystectomy, at a time when the sphincter is known to be incompetent (19) It is also known that dilatation of the ducts occurs following implantation of the common duct directly into the intestine (2, 7), and following cholecystoduodenostomy (11) Under such conditions the action of the sphincter is eliminated On the other hand, when the common duct is implanted obliquely so that the duodenal musculature may act as a sphincter, no dilatation results (2) It is interesting furthermore that, in our series, the animals which developed dilated ducts following the operation generally had a lower intramural sphincter resistance than the dogs whose ducts were normal in size These facts seem to indicate that *pressure transmitted into the common duct from the duodenum*, as a result of incompetence of the sphincter may be an important factor in the production of dilatation in many instances

Since the presence of an incompetent sphincter favors regurgitation from the duodenum (10), the possibility of an ascending infection must be considered Our evidence indicates, however, that the hepatitis which develops is so slight that it is probably of no clinical significance, at least it cannot be detected by the commonly employed liver function tests However, a pre-existing hepatitis may possibly be exaggerated

It is now almost universally agreed that there is no formation of a new gall bladder at the site of the cystic stump as suggested by Lapenta, Eisendrath and Dunlavy, and others Any dilatation of the stump is merely a part of the general dilatation of the ducts

As we have pointed out previously (10), if the gall bladder has been so permanently injured by pathological processes that it does

TABLE I

Dog number	Time interval between operation and sacrifice—in months	Circumference of the common duct—in millimeters	Intramural sphincter resistance—in centimeters of water
1	9½	5	75 0
2	12	5	68 0
3	11	6	40 7
4	10	7	37 0
5	10	7	27 6
6	11	8	41 7
7	11	8	25 0
8	15	10	21 0
9	10	10	18 5
10	10	10	6 1
11	11	12	25 0

not visualize when the Graham-Cole test is applied from a physiological point of view a functional cholecystectomy has already been performed. Consequently no physiological change or damage would be expected from removal of such an organ and if it be harboring infection or stones, cholecystectomy is certainly indicated

Removal of a *functioning* gall bladder however, leads to physiological and morphological changes in the biliary passages and liver The hepatitis which develops is so slight as to be of little clinical significance, but it is conceivable that the disturbed function and structure of the duct system may account for symptoms of distress which occur in some patients after cholecystectomy (10) and this should deter the surgeon from removing a stone-free gall bladder which concentrates, at least until medical control has been tried.

CONCLUSIONS

1 Removal of a functioning gall bladder results in physiological and morphological changes in the biliary system. Among these changes are (a) slight hepatitis (b) dilatation of the biliary ducts, (c) disturbance of function of the choledochoduodenal sphincter mechanism

2 The hepatitis which develops is so slight as to be probably of little clinical significance. It is not sufficient in degree to be detected by commonly employed liver function tests.

3 Incompetence of the sphincter of Oddi may permit transmission of pressure into the common duct from the duodenum. This transmitted pressure must be considered as a possible factor in the production of dilated ducts following cholecystectomy

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PAGET'S DISEASE (OSTEITIS DEFORMANS) AND OSTEOPOROSIS

Similarity of the Two Conditions as Shown by Familial Background and Glucose Tolerance Studies

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In a previous article it was shown that there is a high incidence of familial diabetes mellitus, familial tallness, and familial obesity in patients suffering from Paget's osteitis deformans It was further pointed out that these conditions are of significance, in that they suggest a constitutional factor as providing an etiological background for the development of the disease

Our interest in osteoporosis was stimulated by the fact that in two families having Paget's disease (two in one family) there was one member in each of these families suffering from osteoporosis

In the one family, the father and mother died of diabetes mellitus, the one son has diabetes mellitus and Paget's disease (Fig 1)[2], one daughter has Paget's disease (Fig 2), and the other daughter has generalized skeletal osteoporosis (Fig 3)

In another family, both parents died of pulmonary tuberculosis, one daughter has Paget's disease (Fig 4), and the other daughter has generalized skeletal osteoporosis (Fig 5) In the first family, the one daughter with Paget's disease has a renal calculus, in the second family both daughters have renal calculi, and in addition the osteoporotic victim has gall stones and a calcified fibroid (Figs 5 and 6)

In a series of 12 patients with Paget's disease we showed that there was a high percentage of familial diabetes mellitus (41 per cent), tallness, and obesity We obtained the same information in 10 cases of osteoporosis

In these 10 cases of osteoporosis, 40 per cent had a diabetic family history (this was definitely verified) 60 per cent had one or more members of the family who were 72 or more inches tall and 90 per cent gave a history of heavy set individuals in the immediate family The weight of these heavy set individuals ranged from 175 pounds to 250 pounds As is so well known obesity and diabetes are frequently associated These data correspond quite accurately with the familial background of the Paget's disease victims, in which we found familial diabetes, tallness, and obesity The number in both groups is small, but if a percentage even approximating these figures in a larger series is maintained, the data will have added significance

Important are the glucose tolerance studies in Paget's disease and osteoporosis Chart 1 shows the composite curves of the glucose tolerance in 10 patients with Paget's disease and the same number who were afflicted with osteoporosis

It shows that in both these diseases in this particular group, the curves simulate those seen in diabetes mellitus Two of the osteoporotic victims have diabetes, one in moderate degree and one mild The patient having a moderate degree of diabetes has a marked osteoporosis of the spine with crushing of the vertebræ (Fig 7) One of the Paget's victims has diabetes Even omitting these, however, we found that the curves still simulate the diabetic type Of interest is the fact that a craving for sweets was found in both groups of patients

All 10 cases of Paget's disease had an elevated blood phosphatase ranging from a low of 11 66 Bodansky units to 167 units, the average being 39 13 units (Normal values 1 5 to 4 Bodansky units)

In the 10 cases of osteoporosis, only 1 case was slightly above normal (6 1 units), the range being from "too low to read" to 6 1 units, the average being 3 09 units

The ages of the Paget's patients ranged from 34 years to 60 years, the average age being 48 years The ages of the 10 osteoporotic patients ranged from 46 years to 57 years, the average being 52 years

[2]Since this was written, the patient has developed a right ureteral calculus

[1]From the Department of Internal Medicine, Harper Hospital.

Fig Family 1 patient 1 Has Paget's disease and diabetes mellitus

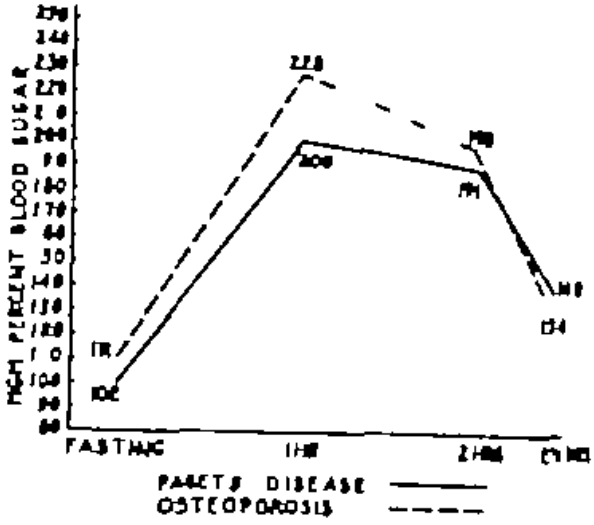

Chart Composite showing glucose tolerance curves

There were 6 male patients with Paget's disease and 4 female In the osteoporotic group there were 2 male and 8 female

Since we are dealing with a disturbed carbohydrate metabolism associated with bone lesions, it is of interest to note that phosphorus compounds are in some way essential to the storage and utilization of carbohydrate, and they are essential to the deposition of bone.

In Paget's disease there is a marked elevation of plasma phosphatase. Phosphatases are enzymes which hydrolyze phosphoric esters such as glycerophosphate and hexose phosphate Phosphatase is present in the growing bone in greatest amount in those areas in which deposition of calcium phosphate is proceeding most rapidly"—(Hunter)

It is also known that the metabolism of phosphorus is closely interwoven with that of calcium.

Another link in the chain of evidence showing that carbohydrate metabolism and phosphatase enzymes are closely related is the experimental work of Schelling He showed that when dogs were depancreatized there resulted a high elevation of plasma phosphatase (40 units or more)

The fact that patients with Paget's disease have a lowered tolerance for carbohydrates and have increased bone formation with a marked increase in plasma phosphatase would suggest that the factor or factors responsible for the carbohydrate metabolism disturbance are also responsible for the bone disturbance with the accompanying phosphatase increase We suggested in the article previously referred to that the pituitary gland may be the responsible factor in producing the disease The well known influence which this gland exercises on carbohydrate metabolism, as well as its definite effect on bone development would make this a logical suggestion We will return later to a consideration of this topic.

As stated before we feel that Paget's disease and osteoporosis are closely related, for they have certain equivalents. Brugsch says that the rebuilding of bone in Paget's disease consists partly of osteoporosis (that is resorption of bone) and partly in excessive formation of new osteoid tissue that may undergo calcification In this sense, he says, the anatomical make-up of Paget's disease is an atrophic hypertrophic osteodystrophy

From this it can readily be understood that there must be a very close relationship between the first process, i e., osteoporosis, and the second the excessive formation of new osteoid tissue

In osteoporosis the bones are undergoing atrophic changes, whereas in Paget's disease the process is similar but goes further in that new bone formation takes place as evidenced by the histological, X ray and phosphatase studies the increased plasma phosphatase being evidence that active bone formation is taking place The difference is therefore that in osteoporosis the disease process is an

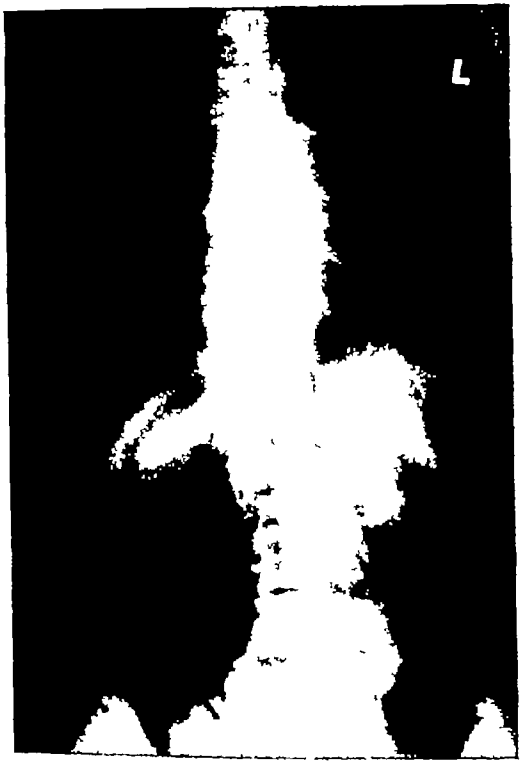

Fig 2 Family 1 patient 2, sister of patients 1 and 3 Roentgenogram shows Paget's disease and renal calculus as indicated by arrow

Fig 3 Family 1, patient 3, sister of patients 1 and 2 Roentgenogram of skull showing osteoporosis

atrophic or destructive process whereas in Paget's disease it proceeds to the hypertrophic state with hypertrophic osteoid formation

So far, therefore, we have several reasons for considering the diseases similar in many respects

1 Paget's disease and osteoporosis may occur in the same family

2 There is a similar constitutional familial background

3 The pathological process is at one stage the same (osteoporosis) in both diseases

4 There is a similar lowered glucose tolerance in both diseases

5 Similar calcium disturbances are shown by the presence of renal calculi in the same family suffering from Paget's disease and osteoporosis

It is obvious however, that there is a fundamental difference in the two diseases for the one disease, Paget s, proceeds to hypertrophic osteoid bone formation which is not true of osteoporosis

Whether this is due to a varying response of the osseous system to the pituitary-parathyroid-calcium-phosphorus relationship is at present unknown

Returning to the discussion of the pituitary gland as the responsible factor in producing these diseases attention is called to the fact that in acromegaly (pituitary eosinophilism) and in pituitary basophilia osteoporosis of the spine is present This is so marked that kyphosis results (Figs 8 to 10)

In both acromegaly and pituitary basophilia hyperglycemia and diabetes mellitus are frequently present In acromegaly the figures for the incidence of diabetes are around 40 per cent Thus the hyperglycemia and the osteoporosis of the spine in these conditions would, according to our opinion, be etiologically related

Rutishauser described 3 cases of pituitary basophilia which he termed "osteoporotic

Fig 4 Family 2 Roentgenogram showing Paget's disease of the pelvis The patient also has a renal calculus

obesity" The osteoporosis is marked and leads to fragility with fractures. In discussing the osteoporosis in these cases Rutishauser says that we know but little concerning the calcium balance in this condition. Aub found an increased output of calcium in one of Cushing's cases. Cushing himself is of the opinion that there is an increased function of the parathyroid

Rutishauser is inclined to ascribe the osteoporosis to the condition of the pituitary gland He gives as his reasons the fact that the pituitary gland exerts such a definite influence on the skeletal system and the bone changes in these cases do not in any way resemble those seen in hyperparathyroidism

In experiments on dogs we attempted to produce Paget's disease by the daily injection of pituitary growth hormone and parathyroid extract. In the dogs receiving these combined extracts massive replacement of the bone marrow by metastatic calcium deposits was present (Fig 11) This was not true of the dog receiving only parathyroid extract We

Fig 5 Sister of patient shown in Figure 4 Roentgenogram shows renal calculus and calcified fibroid as indicated by arrow

Fig 6 Same patient as in Figure 5 Lateral view showing the presence of gall stones and renal calculus as indicated by arrow

were also able to produce calcium deposits in the kidneys of three of the dogs, the largest deposits being found in the two dogs receiving the growth hormone and parathyroid extract (Fig 12) The lesser deposits were found in the dog receiving only parathyroid extract

That renal calculi should be associated with bone diseases is of course a reasonable deduction As is well known nephrolithiasis is found in hyperparathyroidism Recently Albright and Bloomberg again called attention to the frequency of renal stone formation in hyperparathyroidism Castleman and Mallory found renal calculi twenty times in 25 cases of hyperparathyroidism In the two families previously cited, the two female members with Paget's disease have renal calculi and the female member with osteoporosis in the second family has both a renal calculus and gall stones She also has a calcified fibroid In our series of 12 Paget's cases previously reported, 2 of 7 females had calcified fibroids and 2 had renal calculi Of the 10 osteoporotic

Fig 8 Lateral view of acromegalic showing kyphosis

Fig 7 Roentgenogram showing crushing of the vertebræ (This patient has been suffering from diabetes mellitus)

Fig 9 Roentgenogram of spine of patient shown in Figure 8 showing the elongated vertebræ with osteoporosis producing kyphosis

Fig. Photomicrograph of vertebra taken from a case of pituitary basophilia showing marked degree of osteoporosis. Enlarged twenty and one half times. (Courtesy of Dr. Rotshauser.)

patients, 2 had gall stones and 1 had a renal calculus and gall stones. Three[1] therefore had gall stones.

One cannot help but feel that both the renal calculi and gall stone formation are related.

[1] Since paper was written one other patient developed renal calculus.

As we know clinical conditions which are so frequently seen are diabetes mellitus, obesity, cholelithiasis, and nephrolithiasis. Of course the etiology is still unknown, but suggestive at least is the pituitary carbohydrate fat metabolism relationship as well as the previously cited parathyroid-calcium-phosphorus relationship.

In one of the dogs receiving the combined extracts, marked hyperplasia of the parathyroids was found. This substantiates in some degree the work of Hertz and Kraus and Hoffmann and Anselmino who found hyperplasia of the parathyroids following anterior pituitary extract injections. Furthermore the latter workers found an elevation of blood calcium induced by the pituitary extract which was absent following parathyroidectomy. They therefore concluded that the pituitary extract affected the blood calcium through the medium of the parathyroids.

It is noteworthy that in neither Paget's disease nor in osteoporosis is there a variation from normal in the blood calcium. From our studies on the patients with Paget's disease, there seemed to be a tendency to retention of calcium.

All this would tend to support the assumption that there is a very close association

Fig. Photomicrograph showing areas of replacement of bone marrow by metastatic calcium. From dog receiving pituitary growth hormone and parathyroid extract.

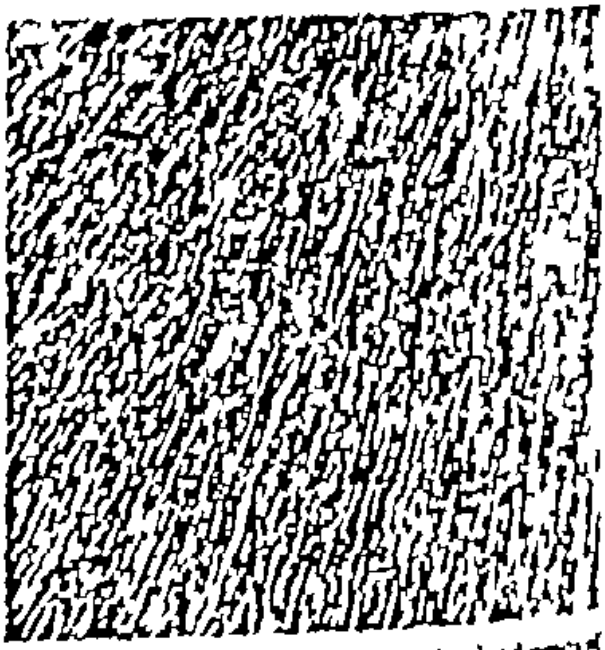

Fig. 2. Photomicrograph of kidney showing deposits of calcium in dog receiving pituitary growth hormone and parathyroid extract.

between the pituitary gland, carbohydrate fat metabolism, the parathyroids, and calcium phosphorus metabolism, and bone formation

Parathyroid extract and calcium act like insulin in lowering the blood sugar (Johnson, Ferrannini, and Moehlig, Murphy and Reynolds) Both anterior and posterior pituitary extracts have a tendency to increase blood sugar and have an antagonistic pharmacological effect on insulin Furthermore, posterior pituitary extract is able to overcome the convulsions induced by insulin hypoglycemia

In this lowered sugar tolerance—bone disturbance relationship, one cannot help but think of Pemberton's findings on arthritis, as he has shown that the arthritic patients have a low sugar tolerance

Because of the familial background and lowered glucose tolerance, as well as the data herein presented, it seemed worth while to treat the osteoporotic individuals like the Paget's cases, namely with a measured carbohydrate diet plus insulin So far we have had very little difficulty in starting Paget's patients on insulin and a diet, but osteoporotic patients are more reluctant to do so because they suffer less

We fully appreciate the fact that the number of cases is small and that a much larger group must be studied before any conclusions can be drawn In regard to the treatment by diet and insulin, we note subjective improvement in Paget's disease The bone pains, sense of pressure in the head, pelvis, tibia, etc , disappear There is also improvement in muscular strength Not enough time has elapsed for us to say whether the disease process is arrested by this form of treatment One patient who has taken a measured diet and insulin faithfully for over 4 months shows a definite advance of the process in the skull His subjective improvement, however, continues We hope to report more fully on this in the future

SUMMARY

In the article it was shown that Paget's disease and osteoporosis may occur in the same family Data were gathered on 10 cases of osteoporosis which showed that there was a diabetic family history in 40 per cent, 60 per cent had one or more members of the family who were 72 or more inches tall, and 90 per cent gave a history of heavy set individuals in the immediate family This corresponds quite accurately with the data obtained in Paget's disease

In 10 cases each of Paget's disease and osteoporosis the glucose tolerance curves were similar, both showing a diabetic type of curve

All patients with Paget's disease had an elevated plasma phosphatase The plasma phosphatase was normal in the patients with osteoporosis, only showed slight elevation

The ages of the Paget's patients ranged from 34 years to 60 years, the average age being 48 years There were 6 male patients and 4 female

In the osteoporotic group the ages ranged from 46 years to 57 years, the average age being 52 years There were 2 male and 8 female patients

The pathological condition at one stage in both diseases is the same, i e , osteoporosis, in Paget's disease the process goes on to the hypertrophic state with hypertrophic osteoid formation

It was suggested that the pituitary gland may be responsible for the two diseases, since it is concerned with skeletal development and carbohydrate metabolism Furthermore osteoporosis of the spine is present in acromegaly and the pituitary basophilia of Cushing

In both these diseases hyperglycemia is frequently present and it is reasonable to assume that the disturbed pituitary function is related to the disturbed carbohydrate metabolism and the osteoporosis More studies on larger series are necessary in order to see if the data gathered on the group represented in this article are borne out If so, there is no question that the etiology of Paget's disease osteoporosis, and other allied bone diseases will be nearer solution Definite subjective improvement is noted in Paget's disease by the giving of a measured diet plus insulin We are not prepared to say whether this form of treatment will arrest the disease process One case receiving this form of treatment for more than 4 months shows progression of the process in the skull although subjective improvement continues More studies along this line are necessary

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LONGITUDINAL OVERGROWTH OF LONG BONES WITH SPECIAL REFERENCE TO FRACTURES

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So well controlled is the normal longitudinal growth of long bones that opposite extremities constantly maintain almost equal length throughout the period of growth Of the factors and mechanism by which this control of rate and duration of growth is accomplished, we have relatively little information except for certain data concerning the influence of certain endocrine glands It is evident that the influence of growth hormones must necessarily be a generalized one and the effect, therefore symmetrical That the growing portions of bone (the juxto-epiphyseal portions of the diaphyses) are responsive to other influences and certainly to one which can alter growth in one or more bones independently of the rest of the skeleton is manifested repeatedly in clinical deformities But since these localized disturbances of growth are observed only in association with pathological states, it does not follow that the factor responsible for them plays a part in normal growth Depending upon the character of this local influence, growth will be accelerated or retarded and result in either asymmetrical overgrowth or shortening Evidence, both experimental and clinical, will be presented to show that these localized alterations of normal growth are probably always caused by a prolonged abnormal state in the blood supply of the growing portions of bone, either a prolonged relative hyperemia or ischemia

Many surgeons have had the gratifying experience of observing in a child an extremity, which is 2 or 3 inches shorter than its fellow as a result of union of a fracture with overriding of fragments, show accelerated growth, so that months or years later both extremities again are equal in length It has also been observed that if union takes place without shortening or with only a small amount of shortening, the fractured extremity may ultimately become considerably longer than its fellow Reported in the literature are numerous illustrative cases and a few in which a shortening as great as 3½ inches has been regained This interesting phenomenon gives rise to speculation Is the shortening overcome by lengthening at the fracture site or by acceleration of the rate of normal growth at the epiphyseal line? If the latter, is it a response to a hormonal or to some other remote regulatory mechanism or merely the result of local factors associated with the trauma and the repair of the fracture?

An experimental investigation of this problem follows

REPORT OF EXPERIMENTS

Twenty-five kid goats were used and all were less than 3 months old when subjected to the initial operative procedures All operations were performed with rigid aseptic technique and all but one wound healed by primary intention Two goats died, one from accidental injury 2 months after operation the other from unknown cause 1 month after operation In all animals in which a fracture had been produced, the fragments were maintained in the desired position by dressing the extremity in a non-padded plaster cast To assure accurate maintenance of position, the fragments were carefully held by an assistant while the wounds were closed and the cast applied Immobilization was maintained for 3 weeks at which time firm union had taken place in each instance Comparative measurements of growth of both the operated upon and control extremities were made from roentgenographic records which were obtained immediately after operation, then at monthly, and later at longer intervals until the experiments were terminated These roentgenograms were made with a precisely constant technique and with the lateral surface of the extremity in intimate contact with the film The tibia is so superficial on its lateral aspect that error in measurements from distortion would be negligible However, the measure-

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Fig 1 Experiment I A Goat 36 From left to right ( ) and ( ) Tibiae of goat 2 weeks old ( ) Fractured left tibia with no shortening Plaster cast immobilization ( ) Normal right tibia (3) Left tibia 4 weeks later fragments have slipped and united with overriding causing shortening of 3 5 millimeters (4) and (5) Fractured left and normal right tibiae 77 days after operation Note only millimeter of shortening The chart shows the differences in length in the two extremities at monthly intervals over a period of 6 months By the end of the first month, there was shortening of 3 millimeters This was regained during the next month and for month both extremities were the same length During the fourth and fifth months the fractured tibia became 2 5 millimeters longer than the control, but during the sixth month this and an additional millimeter were lost terminating in a shortening of millimeter

ments from which the results of the experiments were determined were obtained directly from the postmortem specimens

EXPERIMENTS

Series I Shortening from Overriding of Fragments

In this group of experiments there was reproduced the condition encountered in clinical fractures in which union takes place with the fragments overriding

Experiment A In kid goats, approximately 2 and 3 weeks of age, shortening was produced in the left tibia by causing overriding of fragments In 1 animal, this was brought about deliberately in the other unintentionally from slipping of fragments in a too loosely applied cast As shown in Figure 1 the slipping did not occur until after the first film had been made, which was several hours after the cast had been applied

In each animal the shaft of the left tibia was exposed and fractured by a transverse saw cut The right tibiae were not disturbed and served as strictly normal controls Immobilization was maintained in a plaster cast for 3 weeks, union in each instance being firm at the end of that time Measurements of growth were made from periodic roentgenograms and from the postmortem specimens The results are shown in Table I and those of one goat are illustrated in Figure

Actual measurements of the entire length of postmortem specimens were, fractured 205 5 millimeters, control 207 millimeters The shortening which originally 3 millimeters had become reduced to 1 0 millimeter a final gain of only 1 0 millimeters The original shortening of 3 millimeters was regained in the second month and both tibiae remained equal in

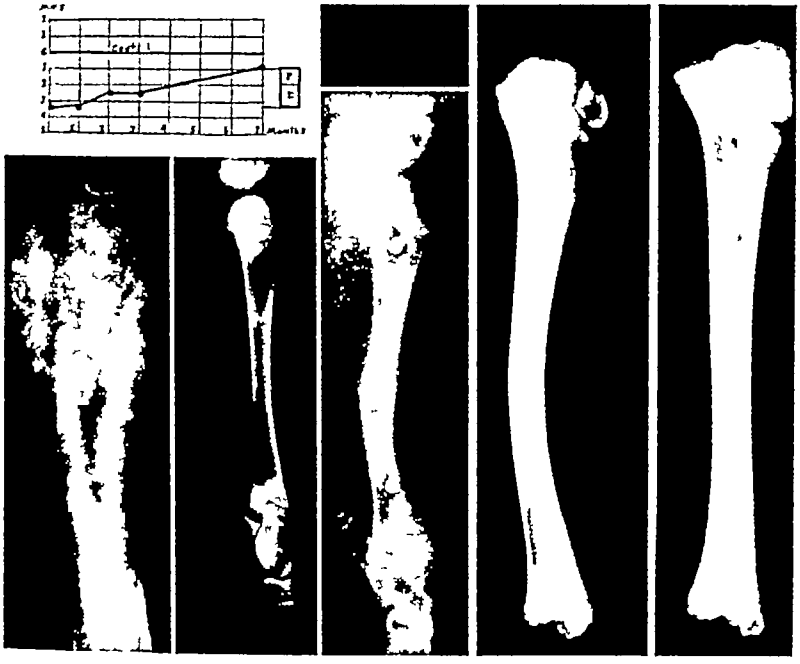


Fig 2 Experiment I B Goat 34 From left to right (1) and (2) Tibias of goat 10 days old with ends of the shafts marked with shots placed in drill holes in the cortex, left tibia fractured and overriding with shortening of 3 5 millimeters Plaster cast immobilization Right tibia is the control (3) Left tibia 8 weeks later (4) and (5) 215 days after operation shortening of only 1 millimeter The chart shows the progressive reduction of shortening from 3 5 millimeters to 1 millimeter over a period of 7 months *P* and *D* designate proximal and distal ends of the fractured tibia and show the amount of the reduction of shortening which took place at the respective ends 1 millimeter from the proximal and 1 5 millimeters from the distal This was determined from the shots which have maintained fixed points that mark the positions occupied originally by the ends of the shafts from which growth is measured Note that the shots have remained equidistant showing that all growth has occurred at the ends

TABLE I —GOAT 36

Days after operation		0	28	57	87	111	140	177
Length of tibia in mm	Control	91 5	99	107 5	1 1 5	135	150 5	152
	Fractured	92	96	107 5	121 5	135 5	151	151
Shortening in mm		(0 5)	3	0	0	(0 5)	1 (1 5)	1 0
Increase in mm			lost (3 5)	3	0	0 5	0	1 0 (1 5)

length for the next 2 months then the fractured bone gained 5 millimeters During the next 4 months the growth was retarded with a loss of 4 millimeters so that in overgrowth of 2 5 millimeters by the end of 7 months, terminated 5 months later in a shortening of 1 5 millimeters

In goat 35 an original shortening of 3 millimeters was regained by the end of 5 months followed by an overgrowth of 1 5 millimeters by the end of the fifth month During the next 5½ months growth proceeded at an equal rate from both tibias so that the fractured tibia was 1 5 millimeters longer than the control at the termination of the experiment 8½ months after operation Thus the maximum gain of 4 5 millimeters was retained constantly during the last 3½ months of observation

Experiment B To determine from what portion of the fractured bone overgrowth occurs, fixed points from which measurements could be made were established in the shafts of both the control and fractured tibias in twin goats 10 days old This was accomplished by placing steel shots into both proximal and distal ends of both tibial shafts The anterolateral aspects of the ends of the shafts were exposed holes drilled at measured distances (a few millimeters) from the epiphyseal lines and into the holes were placed oversize shots which fitted snugly and protruded slightly from the external cortical surface The epiphyseal lines were not exposed, thus avoiding the danger of growth disturbance from this cause but were located by means of sounding with a fine needle

The mid shaft of the left tibia was then exposed and fractured transversely by means of a saw cut

Overriding of fragments and consequent shortening was deliberately produced in one animal and unintentionally attained in the other from slipping of the fragments during application of the cast

The results of the experiment in one goat are shown in serial roentgenograms in Figure 2 and in Table II

TABLE II —GOAT 34

Interval after operation in days			30	6	90	175
Length of tibial shafts in mm	Control	96	103 5	5	13 5	98
	Fractured	85	90	5		167
Shortening in mm		2 5	2 5	5	5	
Length gained in mm						5

The actual measurements of the entire length of the autopsy specimens were fractured 188 millimeters, control 189 millimeters. An original shortening of 3 5 millimeters was reduced to 1 millimeter, a gain of 2 5 millimeters, of which 1 5 was gain at the distal end and 1.0 at the proximal end

In goat 37 an original shortening of 9 millimeters had become reduced to 7 5 millimeters at the time of accidental death 75 days after operation. This gain in length of 1 5 millimeters took place principally at the distal end.

In this series of experiments as in those that follow the total lengths of each pair of the other principal long bones (the femur and metatarsals of both the operated upon and the control extremities) were compared and found to be equal. In this and in each experiment in which the end of the bones were marked with shots, measurements showed that the shots remained equidistant from the beginning to the termination of the experiment. It is apparent, therefore that the reduction of shortening of the fractured tibias was accomplished by an acceleration of the rate of growth that no length was gained at the site of fracture and that the factor responsible for the accelerated rate of growth was strictly local in its effect influencing not even the other bones of that extremity

It may be argued that the presence of the shots near the epiphyseal lines might influence growth to the extent of invalidating the experimental results But since shots were placed in both the operated upon and control bones, any effect that they might have resulted should be equal in both bones and thus would not cause error in results based upon comparative measurements Also it should be noted that the same procedure carried out without the use of shots in the first experiment of this series gave rise to slightly greater acceleration of growth so it would appear that shots influenced growth little if at all.

Series II Shortening from Block Resection

Since it is impossible to determine accurately the amount of shortening which resulted from overriding of fragments in the foregoing experiments, the following procedure was carried out in 3 kid goats, 6 8, and 12 weeks of age

Experiment A Both ends of both tibias of each animal were marked with steel needles as described above Then a segment of the shaft of each right tibia was removed and the fragments were brought together with shortening equal to the length of the segment removed These were 24 26, and 27 millimeters long Each excised segment was split longitudinally into three pieces which were used as grafts to bridge the fracture lines, one applied as an intramedullary peg and two as onlay grafts The position was accurately maintained by an assistant until the wounds were closed and non padded plaster casts applied

In one goat the intramedullary peg slipped down into the distal fragment permitting angulation and malalignment. The proximal fragment eroded and protruded through the skin and a small segment of it sequestrated. Consequently data from this animal was not used In the 2 others, union took place with end-on apposition and with good alignment Roentgenographic records were made immediately after operation, 3 weeks later after removal of the casts, and periodically until the animals were killed 11 months after operation Data from these and from the actual measurements of the postmortem specimens are shown in Table III Illustrative roentgenograms of one animal, goat 28 are shown in Figure 3

TABLE III.—GOAT 28

Days after operation			35	69	104	300	300
Length of tibial shafts in mm	Control	175	135 5	33	32 5	177	190
	Fractured	160	36	134	34	138	175 5
Shortening in mm		15	19 5	19	19 5	16	16 5
Length gained in mm			3 5	5			5

From actual measurements of the postmortem specimens the total lengths were: control tibia 205 5 millimeters, and fractured 190 millimeters.

The original shortening of 15 millimeters in the right tibia became reduced to 16 5 millimeters, representing a gain in length through acceleration of growth of 8.5 millimeters Of this gain, 6 5 milli-

Fig 3 Experiment II A. Goat 28 From left to right (1) and (2) Tibias of a goat 8 weeks old, both ends of both shafts marked with steel needles The left has been fractured and shortened 25 millimeters by resecting a total segment of the shaft which was split longitudinally into three pieces and used as grafts, immobilization in a plaster cast. The right is the normal control. (3) and (4) Show the same tibias 2 months later and (5) and (6) 10 months later The chart shows that the original shortening of 25 millimeters was reduced to 16 5 millimeters The greatest gain took place in the first month That most of the gain occurred at the distal end is shown in the column marked *P* and *D*, proximal and distal.

meters occurred at the distal end and 2 0 millimeters at the proximal end Most of the overgrowth occurred during the first month

Goat 27 In this experiment, the right tibia was shortened 26 millimeters by resecting a segment of the shaft of this length During 11 months of growth, 10 millimeters were regained so that there remained a residual shortening of only 16 millimeters of which 6 millimeters were gained at the distal end and 4 millimeters at the proximal end

Experiment B In two kid goats 8 and 12 weeks old, the procedure just described was repeated with the exceptions that the right tibias were shortened 34 and 38 millimeters, the resected segments were discarded and not used as grafts and the fragments were fixed in approximation with Lane plates This was done to determine whether the presence of a plate would have an added influence upon the rate of growth and also to fix the fragments so that lengthening could not take place at the fracture site, it being conceivable that length could be gained from deposition of new bone between the fragments It is obvious that this did not occur in the foregoing experiments from the fact that the markers in the bones had remained equidistant throughout the period of observation and that the gain in length could always be accounted for at the ends of the diaphysis distal to the markers

One goat died a month after operation from an accidental crushing injury of the chest so that data was collected only from the one remaining Serial roentgenograms are illustrated in Figure 4

TABLE IV —GOAT 29

Days after operation		0	34	73	110	195	308
Length of tibial shafts in mm	Control	148	154	165	177	187	206
	Fractured	110	115	131 5	145	155	176
Shortening in mm		38	39	33 5	32	32	30
Length gained in mm			Lost 1	5 5	1 5	0	2

The total lengths of the tibias at postmortem examination were control 222 millimeters, fractured 192 millimeters A shortening of 38 millimeters was reduced to 30 millimeters, a gain of 8 millimeters, 5 millimeters were gained at the distal end and 3

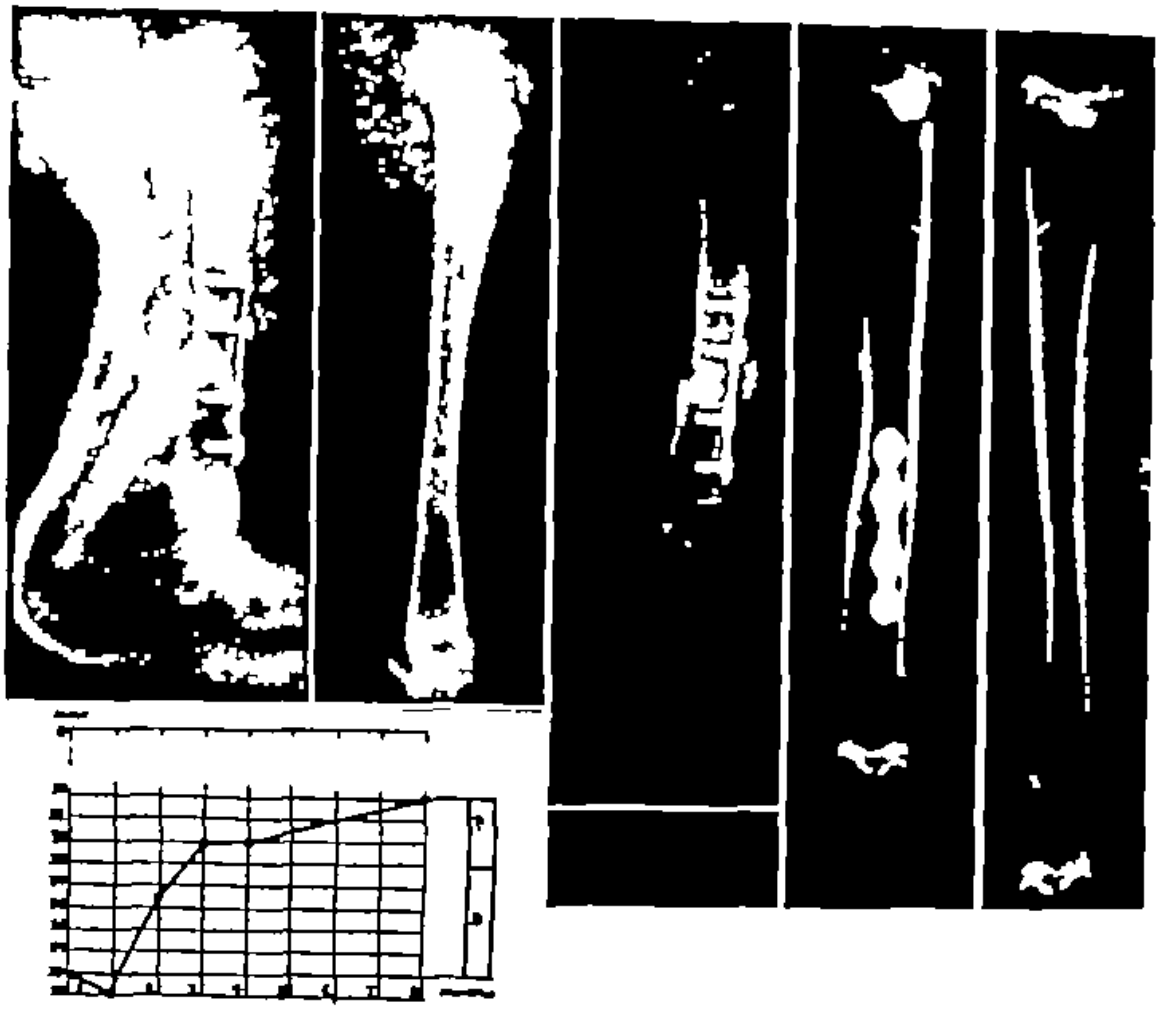


Fig 4 Experiment II B Goat 30 From left to right ( ) and ( ) Tibias of goat 8 weeks old with both ends of both shafts marked with steel needles, the left has been shortened 38 millimeters and the fragments fixed with a bone plate Immobilization in a plaster cast The right is the normal control (3) The shortened tibia month later and (4) and (5) both tibias 8 months later The chart shows that the original shortening of 38 millimeters has been reduced to 30 millimeters and that the major portion has occurred at the distal end (*P* and *D* indicate proximal and distal) Note that most acceleration of growth occurred during the second nd third months

millimeters at the proximal end During the first month the shortening was increased 1 millimeter but during the second month 5 5 millimeters were gained The major gain took place during the second month

In this series an exact measured amount of shortening was produced as a basis from which to determine the additional length gained from an acceleration of the rate of growth which proved to be uniformly greater than in the other series of experiments. To account for this larger overgrowth two explanations are possible The original shortening was much greater creating therefore a greater demand for compensatory acceleration of growth More plausible is the assumption that a more extensive and prolonged disturbance of circulation occurred as a result of the more extensive operative procedures and had a greater and longer stimulating effect upon growth.

It is interesting to note that the needles which were placed at right angles to the long axis of the shaft became oblique as growth progressed as does the nutrient canal of each bone.

Series III Fracture With No Shortening

In all of the foregoing experiments, observations were made of extremities in which a bone not only was fractured but also was shortened as a result of the fracture. To eliminate the influence of shortening and to

[illegible]

[illegible]

The total length of the tibia obtained at autopsy were fractured [illegible] millimeters control [illegible] millimeters. As a result of an acceleration in the rate of growth the fractured tibia became [illegible] millimeters longer than its normal fellow. Almost the entire gain in length was made at the distal end. The greatest gain occurred in the second month.

In point 10 the fractured tibia was [illegible] millimeters longer than the opposite normal (control) tibia by

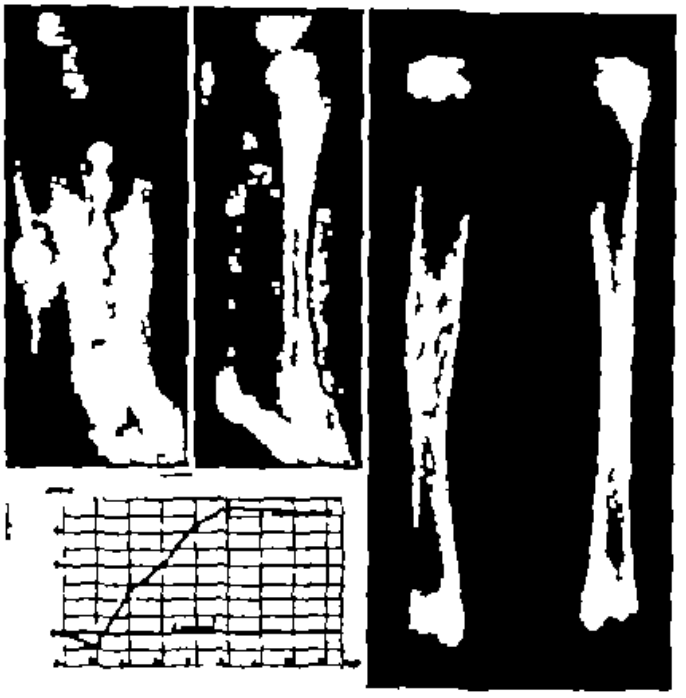


Fig. 6 Experiment III, B Goat 33 From left to right are both tibiæ of goat at ages month and 8 months A fracture without shortening but with internal fixation has resulted in overgrowth so that it has become 7 5 millimeters longer than the opposite normal tibia N markers were used

The chart shows that the greatest gain occurred during the second month

the end of the period of observation 7 months after operation The maximum gain of 2 millimeters occurred in the second month 2 5 millimeters were gained at the distal end, 1 millimeter at the proximal end

Experiment B By the procedure just described the left tibia of a male goat 4 weeks old was fractured transversely and the fragments secured in end-on apposition with a Lane plate, so as to maintain the original length of the bone The experiment differed from the preceding one in that no steel shot markers were used and that internal fixation was utilized Roentgenograms taken at the beginning and at the termination of the experiment 7 months later are illustrated in Figure 6 The measurements were as follows

TABLE VI —GOAT 33

Days after operation			43	44		[illegible]	148	
Length of tibial shafts in mm	Control		38	135	148	17 5	173 5	198
	Fractured	13	137	137 5	151	164	184	195
Lengthening in mm				2		0 5		6
Length gained in mm			Last	1	2	1		Last 1

The total lengths of the tibiæ obtained at autopsy were, fractured 233 millimeters, control 226 millimeters Thus the fractured tibia was 7 millimeters longer than the normal (control) One millimeter was lost in the first month and the maximum gain took place during the second month

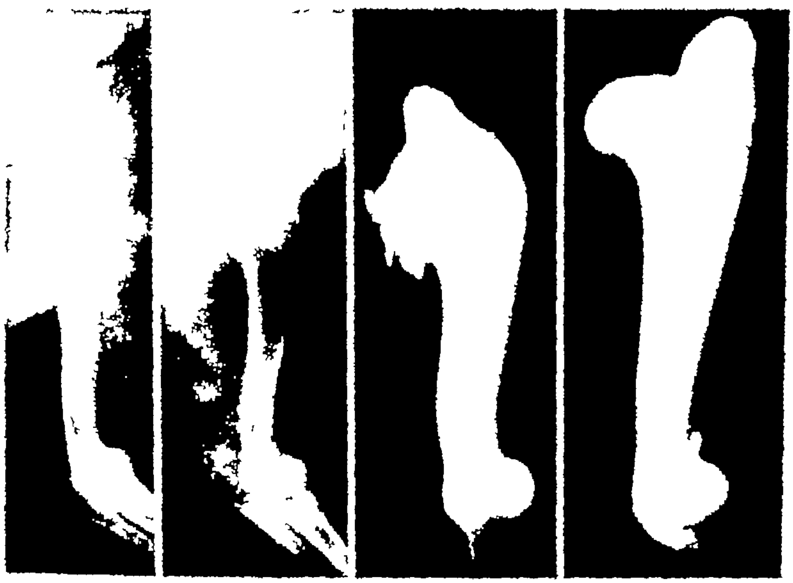
In this group of experiments an acceleration of the rate of growth occurred in fractured bones which were never shorter than the opposite normals and since shortening never existed it is impossible to explain the overgrowth upon the basis of a compensatory adjustment. The acceleration of growth was confined solely to the fractured bones, the other bones of the extremity grew at the same rate as those of each opposite or control leg Measurements of the marked bones show that all of the overgrowth took place at the ends of the bones

It is obvious that a fracture incites in a bone the same abnormal increase in its rate of *growth, irrespective of its length, and that the* responsible factor is local in its action affecting only the involved bone

Series II Shortening from Growth Arrest

The investigation thus far has dealt only with the longitudinal growth response to shortening in bones in which there has been a break in continuity If we assume that the abnormally accelerated rate of growth which occurred had been provoked by some compensatory regulating mechanism, this same response should occur in the presence of shortening regardless of cause.

Thus in each of 3 goats, 4, 4 and 10 days old, shortening of one extremity was produced by arresting growth from one end of one bone from the proximal end of the right humerus in 2 animals and from the distal end of the right tibia in 1 Growth arrest was accomplished by exposing the epiphyseal line and removing as much of the cartilage as possible without producing an epiphyseal separation Bone grafts were then mortised across the line on opposite sides after the method of Phemister The resultant fusion between the epiphyses and diaphyses promptly arrested growth Both ends of the shaft of each of these three bones were marked with steel shots placed at measured distances from the epiphyseal lines The fellow bones of the contralateral extremities were used for controls, marking only the distal ends of the two humeri and the proximal end of the tibia The experimental procedure is portrayed more clearly in Figure 7 than is possible by description Also illustrated is the result obtained in 1 of the animals and this result is consistent with that obtained in the others



... the start of the normal control tib... The arrested tibia grew only ... half of th... arrest at the prox... the same amount of length ... at the proximal ends of both bones.

Thus in each instance growth promptly became arrested at the fixed end and after 15 months there developed shortening equivalent to the loss suffered at the end from which growth had been arrested. The amount of growth from the unarrested end of each bone was almost precisely the same as that from the same end of each fellow (control) bone, that is, equal growth took place at the distal ends

of each pair of humeri and at the proximal ends of the one pair of tibiae. At autopsy the other long bones of the shortened extremity in each animal were compared by measurements with the same bones of the opposite (control) extremity and found to be equal in length. From the beginning to the end of the experiment, each pair of shots (in bones containing two) remained equidistant, showing as in foregoing experiments, that no length had been gained along the shaft, but all at the ends. It is apparent that no attempt was made to offset the progressive shortening which resulted from growth arrest. There was no evidence of a compensatory acceleration of growth at either the unarrested end or in the other long bones of the extremity. From these observations, it can be deduced that there is no general mechanism by which the body is capable of causing an acceleration of growth in a limited portion of the skeleton. The apparent adjustments of discrepancies in length of extremities are probably always merely incidental and the result of local factors.

Series I. Neurocirculatory Disturbances

The experimental observations thus far indicate that growth depends to a very large extent upon the state of the blood supply of the growing portion of bone. This series of experiments was designed to test the influence of gross disturbances in the circulation of an entire extremity.

Experiment A. In 3 kid goats approximately 2, 3, and 3 weeks old, both the femoral artery and vein of one leg were ligated just below Poupart's ligaments. No gangrene or other evidence of circulatory disturbance except for transient coldness of the leg developed and during the period of observation of 7 months growth of all long bones of that extremity in each animal progressed at the same rate as did those of the control or opposite normal extremity. There was no difference in the length of the bones on the two sides at postmortem examination.

In 2 goats approximately 4 weeks of age the external iliac artery and vein of one leg were ligated with the same result. In one animal there was a loss of a portion of the hoof.

It would appear that a relatively normal blood supply had been rapidly established through collateral circulation.

Experiment B. In each of 5 kid goats between the ages of 3 and 8 weeks, an anastomosis was made between the femoral artery and vein of one leg. Due to the technical difficulties of working with vessels *of such very small caliber* only two fistulas were obtained and in these, the bruit which was palpable immediately after operation had disappeared on the following day. At autopsies from 4 to 7 months after operation, the vein in each instance was completely *obliterated at the site of anastomosis* and the artery was patent. In all animals, the comparable long bones of opposite extremities were equal in length.

Experiment C. In this series of experiments it would seem appropriate to refer to a previous publication of the author in which it was shown that sympathetic denervation of an extremity does not alter the rate of growth of that extremity. The experiments were carried out in kid goats and a monkey, and denervation was accomplished by resection of the lumbar sympathetic ganglia and trunk of one side.

RECAPITULATION

The results of this investigation may be summarized briefly as follows:

1. Lengthening in excess of normal occurs in growing bones following fracture. The greatest gain in length takes place in the second month, but continues at a much slower rate for at least seven months.

2. The excess length is gained at the ends of the shaft through an acceleration in the rate of osteogenesis, or in other words, an increase in the activity of the processes responsible for normal growth.

3. Excessive growth occurs irrespective of the length of the bone or of the *necessity of* equalizing the length of extremities. If no shortening exists, actual overgrowth results (the fractured extremity becoming longer than the normal one).

4. Since excessive growth is localized to one extremity and usually confined to the fractured bone, it is believed that the stimulus responsible for it is likewise local.

5. Shortening alone *in the absence of a* fracture did not cause an acceleration of growth. Thus it is apparent that if there is a *compensatory mechanism* within the body which is capable of regulating growth in an effort to maintain equality in the length of extremities, shortening alone does not excite *this mechanism*. It must be conceded therefore, that the fracture and the reparative processes supply the stimulus, and it is sug-

gested by the results of the experiments that this stimulus is merely incidental to the prolonged abnormal status of the circulation of the part caused by the fracture and its subsequent repair This contention is also supported by clinical data to be presented

DISCUSSION OF THE LITERATURE

The literature contains several reports of fairly large series of cases in which fracture shortening has subsequently been diminished, completely compensated, or overcompensated From a group of 75 children, 1 to 11 years old, with fractured femurs, David was able to obtain careful follow-up records on 71 In 38 cases, there were various degrees of shortening, which disappeared within 2 to 15 months after fracture

Burdick and Siris observed 118 children with fractures of the femur in which there was a shortening at the time of union of the fracture of ½ to 3 inches In 53, there was no shortening by measurements when seen 1 to 3 years later, in 14 the shortening was diminishing and in 43 there was no change In 5 cases the fractured leg which was longer than the normal at the time of discharge from the hospital remained so, and in 15 cases in which it was the same length or slightly shorter, it subsequently became longer than the normal one Bruns reports 20 instances in children with fractured femurs in which shortening became completely compensated as growth progressed

Truesdell has stated that "fractures of the shaft of the femur in children frequently, perhaps commonly, cause stimulation of the growth in the injured bone" He reported 5 children, 4 with shortening at the time that union had taken place, in all of whom the fractured extremity not only equalled but became longer than the normal one In 1 case observed for 10 years, the overgrowth had persisted

Similar observations have been reported by Hinz, Leavander, and others All commentators have attempted to explain this phenomenon upon the basis of a generalized compensatory mechanism by which growth is purposely accelerated locally to establish equal length of the extremities Contradictory experimental evidence has been presented and equally contradictory clinical data follows

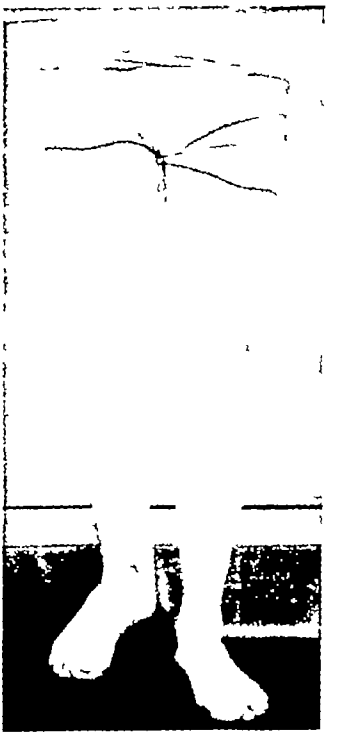


Fig 8 Boy 18 years old with shortening of 2½ inches of the right leg from arrested growth at the distal ends of the tibia and fibula The epiphyseal cartilages have been destroyed by an extension of osteomyelitis of these bones into the epiphyses and ankle joint Since growth arrest of the fibula preceded that of the tibia the foot became deviated into marked valgus

Both femurs were equal in length by both direct and roentgenographic measurements showing that there has been no attempt to compensate in these bones for the shortening

Overgrowth, localized to one bone or to one extremity, occurs in conjunction with various diseases which involve the extremities and despite the great variation in the general nature of these pathological conditions, there is present in all instances one common factor, namely, a prolonged circulatory abnormality of the part, presumably hyperemia The most common of this group are the overgrowths which occur with inflammatory processes of bones, joints or soft tissues adjacent to the epiphyseal cartilage Interestingly, it is in this group that overgrowth was first observed

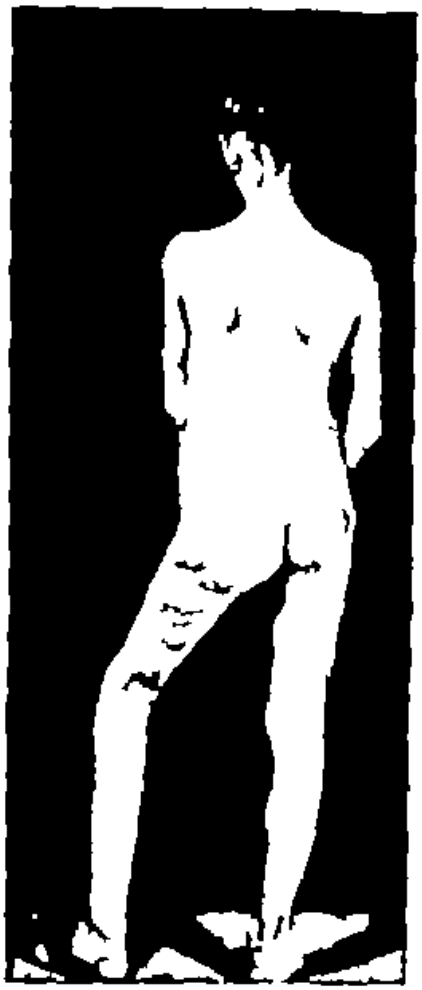


Fig 9 Boy 14 years old with von Recklinghausen's neurofibromatosis The left leg has overgrown and becomes 5 inches longer than the normal right Note large areas of pigmentation typical of this disease.

Stanley in 1849 Paget in 1853 Ollier in 1867 Bergmann in 1868 and Langenbeck in 1869 reported observations of increased length and thickness of bones in which there had been long continued inflammation These inflammatory processes are principally pyogenic osteomyelitis and tuberculous arthritis Helferick reported a gain of 3 centimeters in the length of a leg of a girl 16 years old as a result of merely chronically inflamed superficial ulcers about the knee joint which did not communicate with either the bone or joint Benign and slow growing malignant tumors near an epiphyseal cartilage not infrequently accelerate growth

Certain primary vascular abnormalities almost invariably incite excessive growth in the affected extremity Broca in 1856 reported his observations of a boy 17 years old who had had an arteriovenous fistula of the thigh for 2 years. The leg became 2 inches longer than the opposite normal one. Krause cited a case in which the forearm contained a traumatic arteriovenous fistula and had overgrown 1½ inches Recently Horton reported 23 cases with congenital arteriovenous fistulas of an extremity In 18 there was demonstrable overgrowth.

Israel in 1877 recorded a case in which there was an overgrowth of 5 centimeters in the leg which contained congenital angiectases Since then there have accumulated reports of several similar cases, the overgrowth being confined principally to the bones which contained the hemangiomas

Spinner and others have reported the occurrence of overgrowth in extremities affected with lymphangiectatic elephantiasis.

Spencer Axhausen Stilling, and Grieg, have observed overgrowth in extremities of young growing subjects who have had unilateral varicose veins for a long period of time

As illustrated in Figure 9 localized overgrowth or gigantism is occasionally seen in association with von Recklinghausen's neurofibromatosis. The mechanism in these cases is not clear but is undoubtedly a result of the pathological involvement of the nerve bundles and is, therefore, presumably trophic.

CONCLUSIONS

1 Shortening from overriding of fragments in fractured extremities of children will frequently but not invariably become partially or totally eliminated by the acceleration of growth which incidentally results from the inflammatory process incited by trauma and fracture repair For this reason, operative correction of shortening in these cases should not be undertaken for at least 18 months from the date of fracture

2 Not infrequently excessive growth will cause the fractured extremity to become longer than the normal one. This is more likely to occur as suggested by experimental evidence, in cases treated by open reduction and especially when treated by the introduction of material for internal fixation

3 Shortening from localized arrestment of growth increases until normal growth ter

minates with adolescence There is no evidence that the body attempts to compensate this shortening

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MOVEMENTS OF THE SOFT PALATE

With Special Reference to the Function of the Tensor Palati Muscle

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FOR some years we have been studying the palatopharyngeal valve mechanism and have never been entirely satisfied either with our own interpretations or with the accounts given by others, because up to the present, it has been impossible to observe the palatal movements except from the oral aspect.

Recently we have had the opportunity of observing the mechanism at work from the superior or nasal aspect in a patient who had been the subject of an advanced basal cell carcinoma involving extensively the lateral nasal wall and the orbit. Following excision by our colleagues, Mr. Robert Whillis and Mr. Vernon Ingram, to whom we are indebted for the opportunity of examining the case, the patient was left with a wide opening through the lateral wall of the nose and orbit, through which the whole of the nasopharynx could be examined readily (Fig. 1).

In order that the mechanism may be more clearly understood, it is perhaps helpful first to consider briefly the anatomy of the structures concerned (Fig. 2).

The soft palate is attached to the hard palate in front and to the wall of the pharynx laterally. In the resting stage it hangs downward and backward into the cavity of the pharynx. The space between it and the posterior wall of the pharynx (the nasopharyngeal isthmus) can be varied by the mechanism which will be described subsequently, and this variation is important in speech, blowing, and deglutition. The superior constrictor muscle forms the posterior and lateral walls of this part of the pharynx. There is a gap, the sinus of Morgagni, between the upper edge of the muscle and the base of the skull; through this the Eustachian tube and the levator palati enter the pharynx, and behind these the mucosa bulges out the pharyngeal aponeurosis and buccopharyngeal fascia forming the lateral pharyngeal recess or fossa of Rosenmueller. The cartilage of the tube, covered by mucosa, produces the Eustachian cushion on the lateral wall of the nasopharynx just above the palate. Running down from this to blend lower down with the pharyngeal aponeurosis is the salpingopharyngeus muscle, which, covered by mucous membrane, produces a sharp ridge concave medially on the lateral wall of the pharynx just below and behind the tube.

The foundation of the soft palate is the palatal aponeurosis. This sheet is formed by the spread out tendons of the tensors of the palate. The tensor palati tendon enters the pharynx by hooking around the pterygoid hamulus, piercing the buccinator as it does so. Once in the pharynx it immediately spreads out into a thin sheet attached to the posterior border of the hard palate in front and ending freely behind. Before blending with its fellow of the opposite side this tendon splits to enclose the musculus uvulæ (Fig. 3). Attached to the under surface of the palatal aponeurosis is the glossopalatinus, which forms the anterior pillar of the fauces. To the upper surface of the aponeurosis are attached the levators, the pharyngopalatinus, and those fibers of the superior constrictor which, when they contract, produce the ridge of Passavant on the posterior and lateral walls of the nasopharynx, the so called palatopharyngeal sphincter.[1]

The methods used in the examination of the case were visual observation from above and below, under direct and transmitted illumination. The palate was examined (a) at rest, (b) during speech, (c) during deglutition, and (d) during blowing.

a. *At rest.* It was noted that the transverse measurement of the nasopharynx was about 2 centimeters, and the anteroposterior measurement of the nasopharyngeal isthmus was less than 1 centimeter. These dimensions give a very different impression from that

[1] Wardill, Brit. J. Surg., 1936, 23: 1; and Whillis, J. Anat., 1939, 74: Part 1, October.

gained in the examination of adults suffering from unrepaired cleft palate

b During speech This function is so intimately connected with that of nasopharyngeal closure that we feel the mechanism of this should be first considered

Nasopharyngeal closure is effected at an extraordinarily rapid speed, and analysis is difficult The movements will be described under two headings, and, as far as could be ascertained, in the order in which they occur, namely (1) the contraction of the salpingopharyngeus, and (2) contraction of the levators and synchronous contraction of the superior constrictor muscle with the production of the ridge of Passavant

1 Contraction of the salpingopharyngeus The salpingopharyngeal fold, which in the resting state forms a mere ridge, concave medially, on the lateral pharyngeal wall (Fig 4), straightens by contraction of its contained muscle, forming an outstanding fold just below the cushion (Fig 5) This diminishes to some extent the side to side measurement of the nasopharynx

2 Contraction of the levators and the superior constrictor The most striking feature is the proximity of the insertions of the levator muscles of the two sides into the soft palate In function it would appear that the action is like that of a muscle with two bellies and

Fig 1 Photograph of patient

an intermediate tendon, the latter being the part of the palatal aponeurosis between the two insertions Contraction of the levator muscles (Fig 6) lifts the palate upward and backward, and the two muscles and the intervening aponeurosis act together as a sling drawing the mucosa on the upper surface of the palate almost into contact with that of the posterior pharyngeal wall At the same time the already tense salpingopharyngeal fold

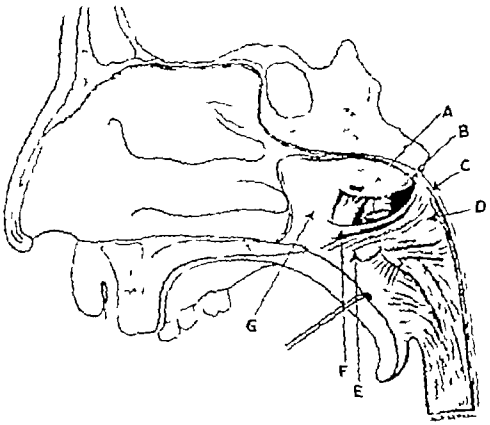

Fig 2 Dissection of normal nasopharynx *A*, Tensor palati, *B*, levator palati, *C*, buccopharyngeal fascia, *D* superior constrictor, *E*, fasciculus passing to soft palate, *F*, fasciculus passing to internal pterygoid plate, *G*, internal pterygoid plate

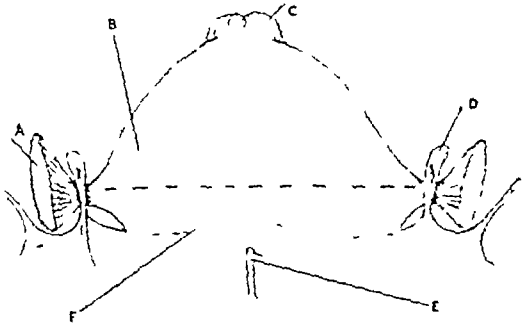

Fig 3 The formation of the palatal aponeurosis by the tendons of the tensor muscles *A*, Tensor palati, *B*, palatal aponeurosis, *C*, musculus uvulæ, *D*, hamulus at medial pterygoid plate, *E*, nasal septum cut, *F*, posterior edge of hard palate

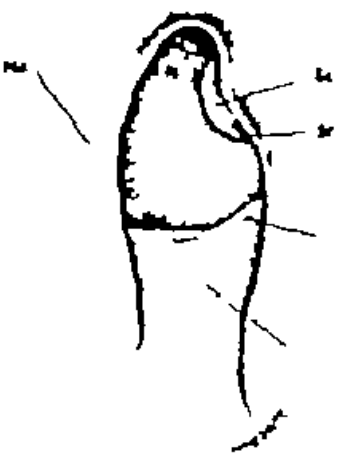

Fig 4

Fig 5

Fig 6

Fig 7

Fig 4 V S Nasal septum E C Eustachian cushion S F salpingopharyngeal fold, L levator eminence P palate

Fig 5 E C S F and L, same as in Figure 4

Fig 6 E C Eustachian cushion, S F salpingopharyngeal fold, L, levator eminence

Fig 7 D The depression which is produced by the tensor

and the Eustachian cushion are pushed upward and backward completing laterally the closure of the isthmus.

Contraction of the superior constrictor At a considerably lower level, and almost out of sight when viewed from the upper surface the synchronous action takes place in the superior constrictor muscle, the transverse fibers contracting strongly in a relatively broad band which comes forward to meet the backwardly displaced palate and at the same time narrowing the whole nasopharynx from side to side

During continuous speech the soft palate rises upward and backward and takes up a position of "ready" in preparation for the more mercurial movements, but yet appears to remain separated a measurable distance from the posterior pharyngeal wall. When speech is rapid and especially when resonance is alternated with explosive consonants, as in such words as "tanner" movement is relatively slight during the opening and closing of the valve, and most of this movement

Fig 8 Coronal section of the soft palate (line A B Fig 3) The dotted outline indicates the position into which the palate is pulled by the tensor 1 Palatal aponeurosis, B muscular uvula C tensor palati, D hamular process

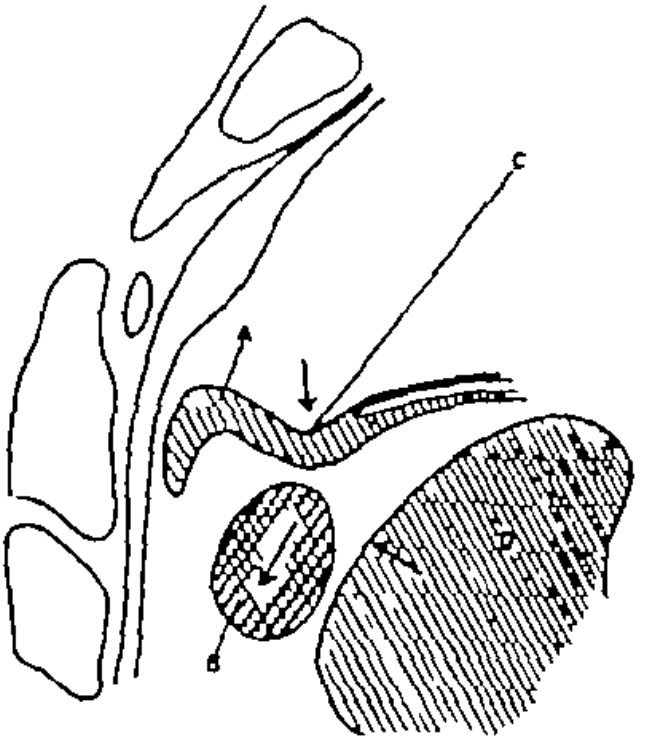

Fig 9 The palate and the tongue appearing the latter into the pharynx A Palate B bulge C groove produced by tensor palati D tongue

appears to take place at a level below the limits of vision It was observed also that certain sounds produce more movement in the palate than others for example the "k" causes the soft palate to rise higher than "t" In general, voiced consonants cause the palate to rise higher than the aspirated consonants

c Deglutition During the act of swallowing the palate rises as in speech, and it was observed that when the bolus reached the back of the tongue in the positions of the tendons of the tensors, dimples appeared on each side indicating that the tensors were contracting to flatten and lower the level of the palatal aponeurosis, and in this way to push the bolus on its journey (Figs 7, 8, and 9) In no other movement of the palate was any action of the tensors seen

d Blowing Inflating a rubber balloon, which necessitates that no air should escape through the nose, produces maximum elevation of the palate and tight bunching together of all the walls of the nasopharynx

CONCLUSIONS

The movements of the palate in all phases of its activity are difficult to interpret and correlate with individual muscles The diameters of the normal nasopharynx are very much smaller than might be imagined from the examination of a series of cases with unrepaired clefts of the palate All movements are extremely speedy and, on superficial examination, little difference is observed between the nasal resonants and the explosive consonants But in general it may be said that the greater the explosive effort required for the production of a sound, the greater is the elevation of the palate and the more firm the nasopharyngeal closure It would seem that closure is considerably assisted by the heaping up of the mucosa by underlying muscles, and it can be imagined that, as has been found in clinical experience complete nasopharyngeal closure is possible even with an almost completely immobile soft palate so long as the sling action of the levators remains intact The tensor palati would appear to have little to do with the speech mechanism, its activity being strongest at the time of deglutition, and it is for this reason that it must be regarded as a muscle, the function of which is to propel the bolus over the back of the tongue

CLINICAL SURGERY

FROM THE MAYO CLINIC

THE TREATMENT OF CARCINOMA OF THE ESOPHAGUS

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ONE of the most discouraging problems in medicine is that concerning the treatment of carcinoma of the esophagus There are many reasons for this justifiable pessimism chief of which is that this lesion represents a very high degree of malignancy and, if all diagnostic and surgical difficulties were solved, ultimate cures rarely would be observed

The fact that malignant growths in the esophagus have advanced to considerable size before producing symptoms, that the organ is inaccessible to surgical approach, that patients who have the disease are usually old and debilitated from lack of food, and that metastasis has occurred in the majority of cases before the disease can be recognized, are other factors that add to this feeling of hopelessness

Although direct visualization of every portion of the esophagus can be obtained through the esophagoscope, early diagnosis" has not been made, and it is questionable whether or not such a diagnosis could be definitely proved if one were fortunate enough to observe a malignant lesion in the early infiltrative stage before ulceration had occurred. Indeed, in cases in which there is an advanced annular carcinoma obstructing the esophagus, with inversion of nearly normal mucous membrane over the growth, it may not be possible to obtain a specimen of tissue for microscopic examination, that will reveal the true character of the lesion.

In few cases in which carcinoma has involved the larynx and the postcricoid portion of the esophagus, the tumors have been successfully resected, and still fewer growths have been removed from the thoracic portion of the esophagus *For the most part, the results from surgical* removal have been disappointing, and in the majority of instances, death has occurred in the course of, or immediately following the operation

It is not my purpose to discourage operations in these cases, but whenever surgical removal is undertaken, the patient and his relatives should understand that the risk is a formidable one, and even if the immediate result is apparently successful, a recurrence can be expected in a majority of cases

The use of radium and roentgen rays has proved of little or no benefit, and in many instances has added to the discomfort of the patient because of nausea and vomiting associated with radiation.

The results from the administration of lead in inoperable malignant conditions in other regions of the body would seem to justify this form of treatment in esophageal carcinoma, but no significant results have been reported. Electrocoagulation of the lesion through the esophagoscope gives promise of producing beneficial results in a few selected cases. In a case recently reported by Moersch, the patient has remained well for 6 months following this type of treatment, and there has not been any local or general recurrence of the growth.

Intubation of the obstructing growth may be accomplished by passing a Rehfuss tube, over a swallowed silk thread, into the stomach and drawing the proximal end through the nose (Figs 1 and 2) or by placing a metal tube such as the one devised by Souttar (3 4, 5) through the growth (*Fig 3*) *I have not used this latter type of tube,* although it has proved of benefit in many cases.

The frequency of hemorrhage and spontaneous perforation in cases of carcinoma of the esophagus should be emphasized to the patient before a tube of this type is inserted into the esophagus Otherwise, if these complications arise in the intubated esophagus, the patient and his relatives may attribute them to the presence of the tube

The two forms of palliative treatment that are most frequently employed are gastrostomy and mechanical dilatation of the stricture (6) The former should never be employed unless diagnosis of carcinoma has been definitely established by

the microscopic examination of tissue removed from the lesion, and it must be remembered that gastrostomy is associated with an immediate mortality of more than 10 per cent Although the insertion of the tube will permit food to be introduced into the stomach, it rarely affords very much comfort, and can scarcely be spoken of as a palliative measure On the other hand, dilatation of the stricture can be accomplished with less than 1 per cent mortality if sounds are passed over a guiding silk thread (Figs 4 and 5a) Undoubtedly, this risk is materially increased if dilatation is attempted without a thread to guide the dilating sounds through the esophagus, or if one were to introduce a dilator through an esophagoscope into the channel of the stricture (Fig 5b) The usual type of thread employed is a size D twisted button-hole silk thread, and the patient is instructed to swallow five yards of thread at the rate of a foot an hour If swallowed too rapidly, the thread will tangle in the esophagus or stomach and the dilating olives cannot be passed over the snarls

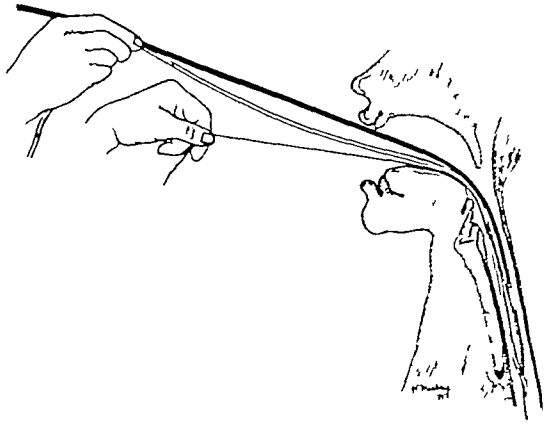

Fig 1 Method of introducing feeding tube into the esophagus over guiding thread

If swallowed properly, it will pass through the stricture in a single strand After entering the stomach and the coils of small intestine, it will

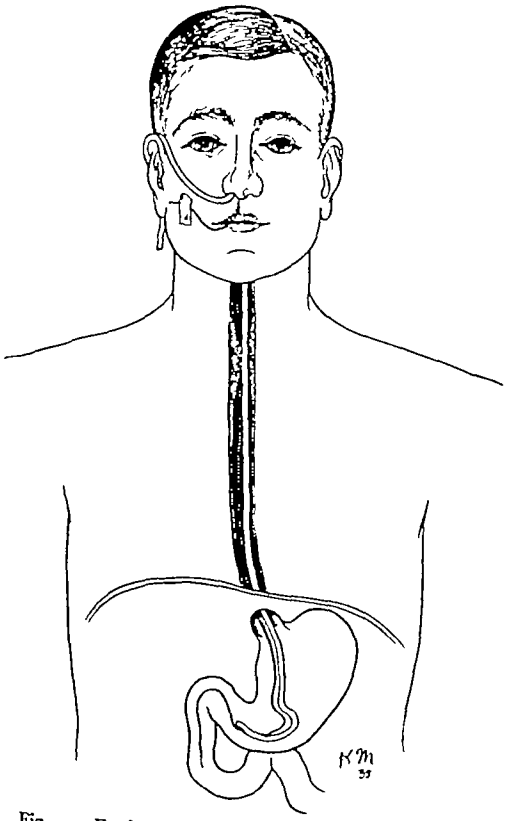

Fig 2 Feeding tube introduced into stomach, with proximal end of tube drawn out through nostril

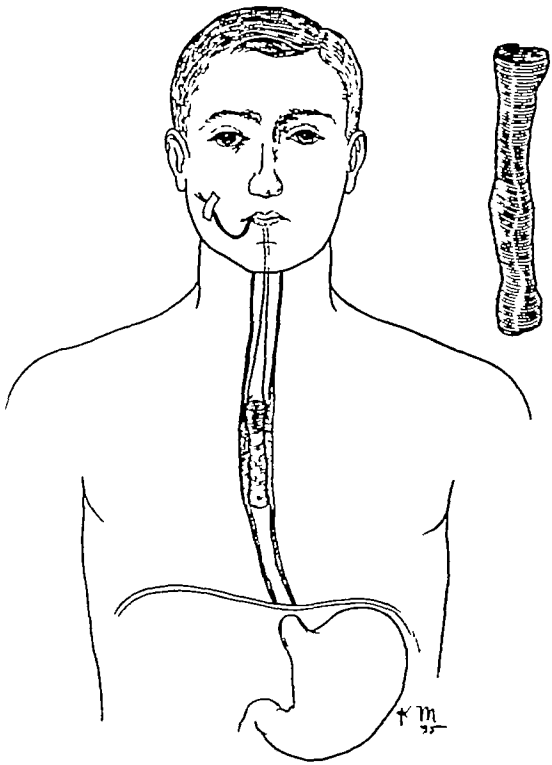

Fig 3 Spiral metal intubation tube devised by Soutta- showing the tube in place in the esophagus

Fig. 4. Typical esophageal carcinoma treated by dilatation, silk thread being used as a guide for passage of the sound

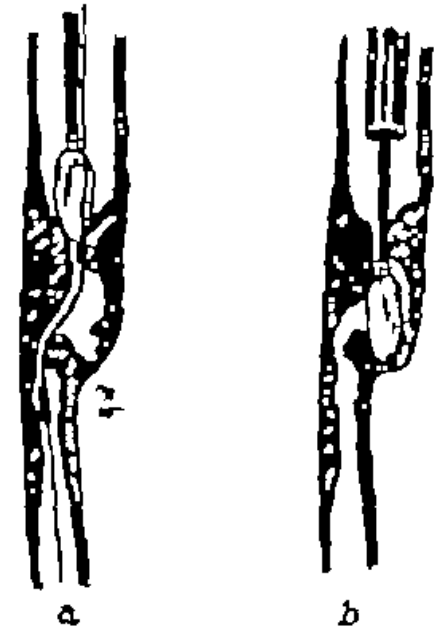

Fig. 5a. Method of introducing dilator over guiding thread, b, same case, illustrating the hazard of attempting dilatation through esophagoscope without guiding thread

become anchored so that it can be pulled taut and used as a guide for passing sounds. More than 90 per cent of patients with esophageal carcinoma are able to swallow soft or solid foods after dilatation with a No. 45 French sound, and this *period of relief usually lasts from 6 to 8 weeks.* Further dilatations will continue this beneficial result for an indefinite period.

In a few instances, patients may have such marked symptomatic closure of the esophagus that they may be unable to swallow a thread, and gastrostomy may be indicated.

Whenever there is pronounced dysphagia, roentgenological examination of the esophagus should be deferred until the patient has swallowed a thread. If this precaution is not observed the barium mixture may completely occlude the partially obstructed esophagus and gastrostomy *may be necessary.*

In the rare cases of esophagobronchial or *esophagotracheal fistula, dilatation should not* be attempted, but recent hemorrhage from the growth is not a contra-indication to stretching of the stricture. The administration of fluids by the rectum or by subcutaneous or intravenous injection should be carried out before dilatation or gastrostomy in cases in which dehydration is present. This procedure may facilitate the *swallowing of the silk thread and certainly will* reduce the risk associated with operation.

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ECTOPIC VAGINAL URETER

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THE ectopic vaginal ureter has thus far evaded the annals of urologic literature except for a few isolated reports It is the object of this paper to correlate the authentic cases, to add one new case and discuss the subject in detail with emphasis on an early diagnosis and treatment

After reviewing many of the cases reported, the author has been obliged to read the original articles for authenticity In many instances the copied reports were found to be incorrect The ureters instead of emptying into the vagina opened around the external meatus in the vestibule, on the labia, or their openings were not definitely located Other reports failed in the history and in the operative findings to give convincing details to warrant this classification Depaul reported the first ectopic vaginal ureter from an autopsy in a newborn child in 1852, while Emmett reported the first clinical case in 1887 Albarran was the first to make a cystoscopic diagnosis in 1897 Of the 22 cases reported 12 have been cystoscoped and only 4 have had a renal functional test The remainder were accidentally discovered at operation or at autopsy

The case which the author wishes to report is unique for two reasons First it is the youngest patient to have recovered and, second the child was relieved by the simplest type of operative procedure yet applied

CASE REPORT

J R. (A 30903), a child of 6 years, had always had incontinence of urine day and night. She voided normally at each urination during the day, about 200 cubic centimeters of clear urine She had always worn diapers and her parents had applied various methods to effect a control of the urine without avail The child herself was beginning to show shyness at school because of her misfortune. Her past history contained an attack of pyelitis when she was 1 year old Her family history was irrevelant

Examination showed a well developed, although rather delicate, healthy child The head, chest, abdomen, and external genitalia were normal The urethra was normal but clear urine was seen to ooze slowly from the vagina The kidneys were palpable at their lower poles but did not appear enlarged or tender Rectal examination disclosed normal pelvic organs All reflexes were considered within normal limits

Laboratory findings The red blood count was 4 5 million with 83 per cent hemoglobin, 6,600 white blood cells and a normal differential and smear The bladder urine was clear, acid, specific gravity, 1 016, albumin, 0, sugar, 0, without casts, pus cells and organisms The vaginal urine was clear, specific gravity, 1 004, with a rare white blood cell and no organisms The phenolsulphonphthalein test was 70 per cent the first hour and 7 5 per cent the second hour None was obtained from the vagina The Kahn test was negative

Cystoscopy was done under nitrous oxide anesthesia after the urethra was dilated The bladder capacity was 200 cubic centimeters The mucous membrane was free from inflammation, tumors stones, and diverticula The ureteral orifices appeared normal as did the trigone and vesical neck Both ureters discharged clear urine They were readily catheterized with No 4 olive tip catheters An intravenous phenolsulphonphthalein test was given which appeared in 5 minutes on the left and 6 minutes on the right with 18 per cent from the left and 15 per cent from the right in 30 minutes Just a faint trace was obtained from the vagina at this time The urines from the bladder and both ureters were normal and free from infection Bilateral urograms disclosed normal kidney pelves, calyces, and ureters with rotation of the right kidney on its vertical axis Additional findings were six lumbar vertebræ and a spina bifida of the first sacral segment (Fig 1) A cystogram was done and found to be within normal limits Acriflavine was introduced into the bladder

Fig 1 Retrograde pyelogram showing normal left kidney and ureter and right kidney pelvis rotated on its vertical axis

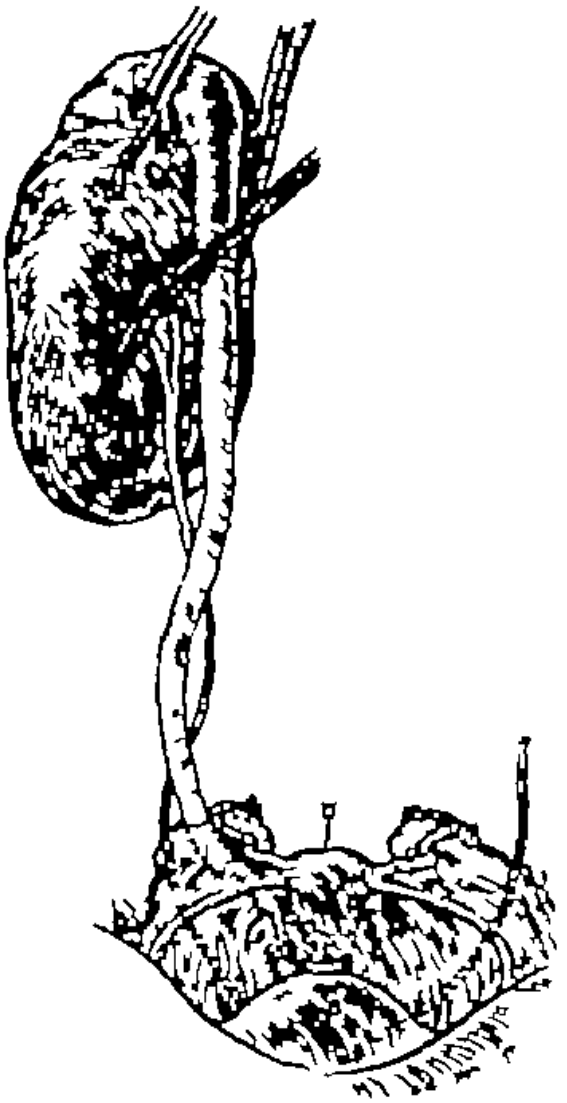

Fig 2 Schematic drawing of right kidney with supernumerary ectopic vaginal ureter *U* Uterus *B* Bladder

but none escaped through the vaginal ost At a second cystoscopic examination indigocarmine was given intravenously A heavy color was obtained within a few minutes from each kidney but only faint trace at the end of 30 minutes was noted from the vagina An intravenous urogram series was executed which did not give any additional information in regard to renal shadows nor were there any evidences of third pelvis A vaginal cystoscopy and endoscopy disclosed the urine to "well-up from the sulcus between the anterior lip of the cervix and the vaginal vault, but the exact opening could not be visualized or catheterized

The author concluded that the child had third ureter which emptied into the upper vagina, but the information as to which side it taught belong could not be ascertained

Operation was done October 8, 933 Under nitrous oxide and ethylene anesthesia both ureters were catheterized and the abdomen was opened in the midline above the pubis A tubular cystic mass the size of finger was found to arise from the right broad ligament and run upward toward the right kidney ventral to the ureter which contained the catheter. The mass portion of the supernumerary ureter protruded into the peritoneal cavity as if by mesenteryy Mercurochrome injected into the lower segment of the large ureter escaped from the vagina. The

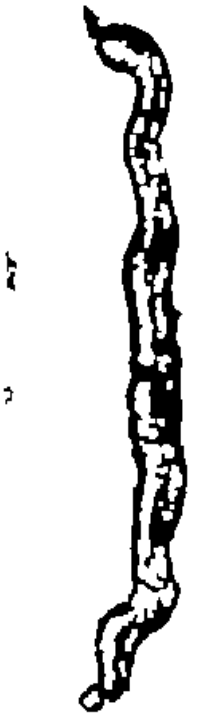

Fig 3 Photograph of ectopic vaginal ureter, right

ureter was then followed down to the cervical neck here it became quite small Here it was cut and ligated Then bilateral wound was closed and second incision was made in the upper right quadrant to expose the kidney and ureter, transperitoneally The large ureter ran to the upper pole of the kidney where moderately dilated pelvis was noted The blood supply was so intricate and as there was no sharp dividing line between the normal kidney and the upper one, it was thought best to do a nephrectomy (Fig) The upper pelvis was firmly ligated with No 000 chromic catgut and the ureter, 1 5 centimeters in diameter and 1 6 centimeters long (Fig 3), was removed in toto This was considered safe because the urine from the ureter was determined to be free from infection The left ureter was found to be normal This incision also was closed without drainage

The convalescence was satisfactory for the first week after which she developed spiking temperature of 100 degrees F for 6 days associated with little vaginal discharge which showed pus and Bacillus coli She did not complain of any pain nor could any tenderness or enlargement of the right kidney be found Rectal examination disclosed no abnormal mass or tenderness The urine remained clear and free from infection The wound healed without any evidence of inflammation, and she was discharged on the twenty second day after operation in excellent condition The vaginal discharge gradually diminished and disappeared entirely in month She has been seen at regular intervals since and appears perfectly well in every ay

CASE REPORTS

ALBARRAN Patient aged 10 years of age he complained of dripping urine in addition to normal urination The urine was found to escape from a small fistula from the anterior vaginal wall. Cystoscopic findings showed a normal bladder and two normal ureteral openings The fistula on the anterior wall of the vagina was 3 centimeters

from the os and was probed for 20 centimeters thereby proving that it did not join either ureter or the bladder The auxiliary ureter was ligated and implanted into the dorsal bladder wall. The bladder and vaginal wounds were closed. Operation was unsuccessful so the large vaginal fistula which did not communicate with the bladder was closed with the *lappenspaltung* principle Patient made a complete recovery

2 ALSBERG Patient was 18 years old and had had incontinence from birth She also voided normally On the front wall of the vagina was a fistulated vesicle which was regarded as a wolffian duct. This was extirpated as far up as the parametrium on the right, but the patient died on the twenty third day of pyemia Autopsy showed that the "vesicle" reached to the right kidney pelvis and was therefore a ureter On the left side there were two normal ureters terminating normally in the bladder

3. CONNITZER. At autopsy bilateral double ureters were found On the left side both ureters emptied into the bladder On the right side, a ureter ran from the upper kidney and terminated in the vagina by a vaginal cyst. The patient apparently died of pyelitis

4. DAVENPORT A woman 29 years of age, the mother of three children, had had incontinence of urine from the vagina and normal urinations all her life The dripping from the vagina varied at intervals She had noticed some thickening of the anterior vaginal wall with a projection for about 2 inches of tissue. On the papilla-like mound of this projection, there seemed to be an opening for the escape of urine. At operation the ureter was separated from the front wall of the vagina and inserted into the bladder A second operation closed the fistula Result recovery

5 DEPAUL. Autopsy revealed exstrophy of the bladder, two completely separate uteri and vaginæ with atresia ani The right ureter ran along the lateral wall of the uterus and emptied into the right vagina by an enlarged opening The left kidney was one-third smaller than the right and was located in the depths of the pelvis The ureter from this kidney also ran along the wall of the uterus and communicated with the vagina by a small opening

6 EMMETT A 30 year old single woman had incontinence of urine with normal urinations The ureter was found to terminate in the upper part of the vaginal wall near the neck of the uterus. At operation a portion of the ureter was dissected out and implanted into the bladder in its normal position Result Ureteral incontinence A ureteroplastic operation was followed by pneumonia and death

7 HERBST AND POLKEY Patient 12 years of age had always had dribbling of urine day and night from the vagina and normal urinations Vaginal examination showed the opening of the vaginal ureter 1 5 centimeters in front of the cervix in the midline on the anterior wall Cystoscopy disclosed a normal bladder with normal right and left ureters Urograms were given as normal. The right kidney was somewhat larger and lower than the left but showed a slightly smaller pelvis. The superior calyx was broad and pushed downward The upper right pelvis was long and narrow and was connected with the vaginal ureter The urines were free from infection from all three ureters. Functional test was not done but the diagnosis was correctly made. The supernumerary ureter was moderately dilated above the lower end Heminephrectomy and partial ureterectomy were done The supernumerary kidney having its own blood supply was removed without disturbing the lower kidney Result cured

8. ISRAEL. A patient, 32 years of age, complained of pain in the left kidney region, frequency of urination, and purulent vaginal discharge. Swelling about the size of the fist developed in the left flank. A diagnosis of suppurative pyelonephritis was made. The abscess was opened and was found to lie not around the kidney but inside the organ It was drained The vaginal discharge stopped After the wound healed, the vaginal discharge began again She had several recurrent attacks X-ray showed that the organ was the third kidney. Insertion of the ureter from the third kidney was thought to be in the vagina but its point was not definitely located. The upper kidney on the left was removed with its ureter Recovery of the patient was slow Histologically, the ureteral wall was found to contain normal circular and longitudinal muscular layers, but the epithelium and subepithelial layers contained numerous round cells The adventitia and connective tissue were very much thickened and fibrous

9 KALLMANN Patient 21 years of age had had a sudden attack of pain in the right lower quadrant. There were no gastro-intestinal symptoms The abdomen was distended The liver, spleen, and kidneys were found to be normal. Vaginal examination was painless The ilocecal region showed definite resistance and was sensitive to pressure The patient was operated upon for appendicitis, but the appendix was found to be normal. The pain became gradually stronger in the region of the right kidney The urine from the bladder, which had formerly been clear, now became purulent as also was that from the vagina. The "subphrenic or retrocecal" abscess was opened The patient's temperature dropped but there was a persistent lumbo-urinary fistula which necessitated a second operation. The fistula was found to have been due to a kidney the upper part of which was pyonephrotic. The urine filled this sac from which escaped an accessory ureter which was also filled with pus The exact location of the termination of the ureter was not found although there was not any doubt that it terminated in the vagina. The kidney was removed The surgical specimen showed two ureters, one of which was greatly enlarged leading to the upper portion

10 H KATZ Case 1 A young woman of 25 years had had incontinence since early youth. The vaginal ureter was found to have an opening on the anterior wall near the hymen Operation disclosed bilateral ureters with the ectopic vaginal ureter on the right. The accessory ureter was implanted into the vertex of the bladder with complete recovery

11 H KATZ Case 2 A single woman of 23 years had always had incontinence of urine. Examination disclosed an opening of a vaginal ureter at the seam of the hymen on the anterior vaginal wall X-ray showed screw-shaped supernumerary ureter on the right with a normal ureter and kidney pelvis on the left. Operation was refused by the patient. After 5 months of gradual diminution in the incontinence, drainage ceased The spontaneous closure is explained on the basis of occlusion of the ureter after injection of X-ray medium. No pain was experienced in the right kidney region

12 KELLEY A girl of 19 years had always had incontinence of urine but had voided normally Examination showed a normal, well developed individual. Clear fluid escaped from between the labia. Cystoscopy showed normal bladder with only the right ureteral orifice Indigo-carmine given intravenously escaped from the right ureteral catheter and from the vagina The source of the vaginal urine was found to be from a small orifice on the anterior vaginal wall 3 centimeters from the vaginal orifice. A No 5 catheter was passed for 12 inches A pyelogram suggested an infantile left kidney Urines were normal from both kidneys. Phthalein test showed 35 per cent in 20 minutes with 3 minutes appearance time on the right and 1 5 per cent in the same time with an

Number Reported by Age	Main symptoms	Opening	Sac	Infection	Cystoscopy	X ray	Operation	Result
Albanese [illegible] 20	Vaginal dripping Normal urine	Anterior vaginal wall	accessory ureter		Normal bladder		1 Nephrectomy [illegible] Ureterectomy [illegible]	Recovery
Alberty 1899 18	Vaginal dripping Normal urine	Anterior vaginal wall at urethra	Right	+	left ureters in blind sac		Extirpation of lower ureter	Died 1st day of peritonitis. Autopsy [illegible] bladder
3 Cameron 1891	Vaginal dripping Normal urine	Anterior vaginal wall at cyst	Right accessory ureter	+	left ureters in blind sac			Autopsy. Died [illegible]
4 Davenport 1890 29	Vaginal dripping Normal urine	Anterior vaginal wall projection	Not given				Separation leaving ureter from vaginal wall Nephrectomy	Recovery
5 Dupuis New born	Extroverted bladder	vagina	Right accessory ureter Left accessory ureter					Autopsy
6 Emmet 30	Vaginal accessory ureter Normal urine	Small opening	Not given				Cystoscopy detected not Nephrectomy	Died of pneumonia. Postmortem
7 Hirst and Pulley 1909 13	Vaginal incontinence Normal urine	Anterior vaginal wall 1 cm. in front of cervix	Right accessory ureter		Normal bladder	+	Hemicolectomy and partial ureterectomy	Recovery
8 Israel 1908 35	Purulent vaginal discharge Normal urine	Not located	Left accessory ureter	+	Normal bladder	+	Pyonephrosis drained Nephrectomy and ureterectomy	Recovery
9 Kellman 1903 11	Pain right side Vaginal urine Normal urine	Not located	Right accessory ureter	+			1. Operation for appendicitis Pyonephrosis drained 2. Nephrectomy both right kidneys	Recovery
10 Kate 45	Incontinence, since birth	Anterior wall near hymen	Right accessory ureter		left ureters in blind sac		Hemicystectomy right	Recovery
11 Kate 30	Incontinence	Anterior wall near hymen	Right accessory ureter		Normal bladder and ureters	+	None	Incontinence disappeared after 1 month
12 Kelley 1911 19	Incontinence Normal urine	Anterior vaginal wall 3 cm. from cervix	Left Infundibulum		Only right ureter		Left nephrectomy	Cured
13 Kennedy-Mackie 4	Pus from vagina Large mass in left flank. Normal urine	Not located	Left accessory ureter	+ Stone	Right accessory ureter in bladder		Mass explorated	Died. Autopsy
14 Kimmel and Orcutt 1913 5	Dripping from vagina. Normal urine	Not given	Right accessory ureter Left accessory ureter		Normal bladder		Right pelvic complicated Left upper ureter completely to close	Recovery [illegible]
15 Lauck 1909 7	Vaginal urine. Normal urine	Not located	Right accessory ureter				Operation for appendicitis Nephrectomy right complete	Recovery
16 Mohan 1903 30	Vaginal dripping Normal urine	Anterior wall 3 cm. from os	Right accessory ureter				Hemicystectomy	Recovery after much pus in bladder
17 O'Connor 1909 38	Partially incontinent	Lateral to cervix, left	Left		Only right ureter	+	Ureter transplanted into bowel	Reported well after 1 yr.

Number Reported by Age	Main symptoms	Opening	Side	Infection	Cystoscopy	X ray	Operation	Result
18. Ottow 1930 32	Incontinence since birth	Anterior vaginal wall	Right accessory ureter	+	Normal bladder	+	1 Neocystostomy, right 2 Left heminephrectomy	Satisfactory
19. Palfin Fetes		2 vagina. Left ureter Left vagina	Left					Autopsy
20. Samuels et al 1922 29	Vaginal urine. Normal ureter	7 mm. in front of cervix on anterior wall	Right accessory ureter	0	Normal bladder	+	1 Operation for vesicovaginal fistula at 6 yrs. no improvement 2 Heminephrectomy, right	Recovery
21. Sargent 1930 23	Incontinent. Normal ureter	Right lateral wall ⅓ way to cervix	Right accessory ureter		Two left ureters one right ureter	+	Two unsuccessful attempts to ligate lower end of ureter, third operation neocystostomy	Clear urine after four months
22. Walz 1931 23	Incontinence	Anterior wall 1½ cm from hymen	Right accessory ureter	+	Normal bladder	+	Complete right nephrectomy	Cured
23. Demmg 1934 6	Vaginal urine. Normal ureter	Anterior wall near cervix	Right accessory ureter	—	Normal bladder	+	Right ureterectomy	Recovery

appearance time of 3 minutes from the left side. A left nephrectomy was done. The kidney showed little functioning tissue, measured 5 5 by 2 6 by 1 centimeter and weighed 11 5 grams The ureter was small The microscopic examination of the kidney disclosed the architecture to be of the infantile type Recovery of the patient was complete.

13 KNOEPFELMACHER. A girl 4 years of age had pain and swelling of the left side She voided normally and also passed cloudy urine from the vagina. Catheterized specimen of urine from the bladder was clear and showed no albumin. There was moderate anemia, enlarged liver and spleen. Below the latter, was an elastic resistant area which could be separated from the spleen.

Rectal examination revealed no evidence of tumor The mass was punctured from the back. Purulent urine with a streptococcal infection was obtained. Pressure upon the vagina from the rectum caused pus to escape from the vagina. Pressure upon the tumor did not cause pus and urine to escape from the vagina. Clinical diagnosis was retroperitoneal abscess with fistula into the vagina Since the urine was clear it was thought that the kidney could not be the origin of the abscess and, since the bones were normal, the retroperitoneal lymph glands were taken as the origin of the abscess. Autopsy showed the left kidney divided into two parts, the upper half was thoroughly abscessed with a pelvis of its own It was enlarged, filled with pus, and communicated with the vagina by means of a distorted and enlarged ureter The lower half of the kidney was free from abscess and from its pelvis there was a normal ureter leading to the bladder The right kidney also had a double pelvis with two separate ureters which crossed and ended in the right side of the bladder The liver was amyloid in type. The exact emptying point of the lower end of the ureter in the vagina was not determined.

14. KUMMEL AND GRAFF Patient, 15 years of age, had four ureters. The patient had constant dripping of urine from the vagina in addition to normal urinations Cystoscopy showed a normal bladder with normal ureter emptying on each side. Examination of the vagina showed a right accessory ureter which was probed without difficulty The left was probed with some difficulty The right kidney was exposed and the pelves anastomosed This was difficult due to the small size of the patient. The left ureter was separated at a later operation, tied off, and brought to the skin The patient completely recovered with a draining sinus on the left.

15 LINCK. Patient, aged 7 years, had an attack of pain on the right side which was thought to have been due to appendicitis At operation, a double right kidney was found The upper kidney was drained and found to contain pus. It drained off and on for some time with a development of an extensive fistula as well as a purulent drainage from the vagina. Complete extirpation of both kidneys on the right was done with recovery The exact location of the termination of the ureter within the vagina was not definite.

16 MILTON Patient, aged 30 years, had always had dripping of urine from the vagina and voided normally She was married at the age of 13 An opening on the anterior vaginal wall ½ inch from the os was found. This was probed in the direction of the right kidney It discharged 2 ounces of urine per day There was no mention of infection At operation the right ureter was inserted into the base of the bladder Convalescence was followed by much pain in the region of the right kidney for a long time but eventually the patient made a complete recovery and was cured.

17 O'CONNOR. A woman of 38 years had always been partially incontinent. She had had gonorrhea and a bilateral salpingectomy 6 years before. Cystoscopy showed only the right ureteral opening Vaginal examination showed urine escaping from an orifice above and lateral to the cervix. This was catheterized and clear urine obtained Indigocarmine output was good Pyelograms showed normal left ureter, calyces, and pelvis The ureter was transplanted into the bowel and the patient made a complete recovery Seven years later, she was reported to be well and no urological study was carried out

18 OTTOW A 32 year old nullipara who had complained of incontinence since childhood was found to have a small opening on the anterior vaginal wall which put out urine but which was too small to allow the entry of the smallest catheter or probe. X-rays showed a double kidney

pelvis on the right with two ureters and a single upper urinary tract on the left. A laparotomy was done and the lower ureter on the right implanted into the bladder after the Fritsch Stoeckel method. Incontinence continued. A second laparotomy was done and an accessory left ureter was found emptying into the vagina and leading to a cherry sized kidney above the normal left kidney but receiving its blood supply from the main kidney. The accessory kidney and ureter were removed. The result was satisfactory. Histological examination showed the left ureter, which was dilated, to be normal while the rudimentary kidney showed few normal glomeruli and tubules with some fibrosis, a calcified area and colloidal deposits in distended tubules. No epithelioma was found at the lower end of the ureter which accounts for some evidence of infection in the kidney (case of bilateral accessory ureters emptying into the vagina)

19. Pallin. Autopsy report of an infant which had two uteri and two vaginas. The left ureter inserted into the left vagina, while the right vagina inserted into the left ureteriae.

20. Kaufmann, Kerr, and Eccles. The patient, a single woman 29 years of age, complained of incontinence. She voided normally but had had day and night urinary leakage from the vagina since birth. At 6 she was operated on for vesicovaginal fistula without success. Menstruation was normal. Vaginal examination showed opening of the right ureter on the anterior wall of the vagina 7 millimeters in front of the cervix. Cystoscopy showed a normal bladder with normal right and left ureteral openings. The urine from each of the bladder ureters ran three times as fast as that from the vaginal ureter. The urine from all three ureters was sterile. The phthalein functional test showed 30 per cent from the right kidney 42 per cent from the left, and 2.5 per cent from the vagina. X-rays showed normal right kidney pelvis and a supernumerary hydroureter. They concluded that the hydro-ureter was the result of the plastic operation. The operation disclosed a supernumerary upper right kidney which was removed as it had separate vessels from the main kidney. The supernumerary kidney was 4 by 4 centimeters. The ureter and blood vessels of the upper kidney passed posteriorly to the vessels of the normal kidney. Microscopically the kidney removed showed perfect pyramids which were dwarfed. The ureteral walls were thickened. Recovery.

21. Emmert. A working girl of 23 had urinary incontinence since birth and also had normal menstruation. She had never had any serious illness. Examination showed normal physical condition except for hypertrophy of labia minora and clear fluid escaping from the vagina. Vaginal examination showed a mucous ridge running on the right vaginal wall and half way back was seen a small opening from which clear urine escaped. This was catheterized for a distance of 5 centimeters. Cystoscopy done at the same time disclosed a normal bladder except for two ureteral openings on the left. All four catheters were injected. The vaginal ectopic ureter ran to the upper right kidney. Phthalein escaped through the vaginal ureter but the amount was not determined. Fifty per cent was obtained from the other three catheters in 30 minutes. Roentgenograms suggested that the upper right kidney was rudimentary. Two attempts were made to ligate the vaginal end of the ureter without success. A third operation was successful, transplanting the lower end of the ureter into the base of the bladder. Although the patient had some febrile reaction, a cystoscopy 4 months later showed an apparently clear urine.

22. Wilhelm Walz. A 23 year old virgin was noted to have incontinence of urine since childhood. By means of a Hirschmann kolposcope a small slit-like opening was found on the anterior vaginal wall 1.5 centimeters from the urethra and slightly to the right of the midline from which escaped at intervals small drops of fluid. This was catheterized for a distance of 14 centimeters. X-rays and cystoscopy revealed an accessory ureter on the right which was dilated and led to a hydronephrotic upper kidney. The left kidney and ureter were normal. There was very little function from the accessory kidney which was affected with Bacillus coli. At operation a complete right nephrectomy was done because the upper hydronephrotic kidney was not sharply defined from the lower normal kidney. Patient made a complete recovery. Microscopic study of the kidney tissue showed evidence of infection.

EMBRYOLOGY

It must be recalled that the ureter develops from the wolffian duct, that the vestibule also develops from the same source, but that the vagina is of muellerian origin. Thus, we may find the reason why so many ectopic ureters empty in the vestibule, being of the same origin. However the shifting of the ureteral opening to another organ demands greater embryological forces. The most logical theory for the supernumerary vaginal opening is based on the fact that instead of a single invagination from the wolffian duct, there are two or more anlagen, each forming a ureter with separate implantation into the kidney. As the wolffian duct shifts with the urogenital sinus downward, it carries the upper ureter with it and causes a lower implantation of the upper ureter. If the two urethral buds develop at the same time they may be found with their openings near together in the bladder but if the upper ureter develops later it may be carried below the bladder by the muellerian duct to empty into the genital tract as in the vagina.

The vaginal opening for these ectopic ureters is practically always on the anterior wall in the midline although, as the opening nears the cervix, it may become more lateral. Three are described as pinpoint openings although one is described with several openings. Three were found near the cervix. Five were not definitely located.

INCIDENCE

The age incidence shows two at birth with various other anomalies of the genito-urinary tracts, 3 more in the first decade, 5 in the second, 9 in the third, 3 in the fourth, and the age on one was not given. The right ureter was involved in 50 per cent of the cases while the left was involved in 25 per cent and bilateral ectopic condition was found in 10 per cent. The side was not mentioned in two reports. In 17 cases the vaginal ectopic ureter was supernumerary on the side involved. In 3 cases the ectopic ureter was a

single left ureter while on the opposite side only one case showed a single ureter The percentages enumerated are probably not exact as not all patients were cystoscoped and the data are insufficient However, it is quite apparent that the right side is the more frequently involved and that bilateral ectopic ureteral openings occur in about one-tenth of the cases on record The Weigert-Meyer theory always holds good as the vaginal supernumerary ureter always runs to the upper kidney

PATHOLOGY

The pathology of the kidney and ureter connected with the ectopic vaginal ureter has never been appreciated The kidneys are usually small and of hypoplastic type with blood supply closely associated with the main kidney. Rarely they may be found to have separate vessels A number of the surgeons write of the difficulty in removing the supernumerary kidney because the vessels are so intricate Only two specimens are described in detail. Grossly at operation most of them have been found to be thin walled sacs with dilated pelves and ureters In the microscopic study of the two uninfected kidneys the renal tissue was hypoplastic The ureters are enlarged with normal histological pictures Whether normal valves exist at the lower end is not as yet determined, although most ureters are described as being constricted at this area The function of these kidneys is insignificant by the phenolsulphonphthalein and methylene blue tests The specific gravity of the urine was very low in the author's case.

It would seem from both the clinical and pathological studies that these supernumerary kidneys do not, as a rule, contain much renal tissue and are very prone to infection which may cause a large pyonephrosis or spread to the lower kidney

SYMPTOMS

The symptoms of ectopic vaginal ureter are quite definite All cases had vaginal dripping of urine day and night. The amount of urine varied somewhat and often was increased when the patient became excited In addition, normal urinations occurred When the ectopic ureters became infected, purulent urine passed from the vagina In 4 cases the symptoms from infection such as pain and elevation of temperature overshadowed the urinary picture to such an extent that the patients were operated upon for appendicitis or renal suppuration Without infection, the patient does not complain of any discomfort within the kidney region The continued incontinence of urine, however, causes shyness and seclusiveness as well as nervous irritability of the patient

Diagnosis of ectopic vaginal ureter should not be difficult as all cases gave a history of vaginal dripping of urine since birth together with normal urinations Careful local examination as to the source of the urine whether it comes from the vaginal os or from around the urethra demands only the acuity of ordinary vision Too often it is taken for granted that the urine escapes from the urethra As to the location of the opening of the ureter within the vagina more difficulty may be encountered Especially is this true in the child where the canal is small Any insertion of an instrument for vision often causes enough pressure to stop function Again, urinary flow from these ureters is slow and intermittent, and they fail to excrete much of any dye that may be injected Where there is a vesicle or cystic pouch leaking urine, the exact location may be more readily suspected However, practically all empty near the midline somewhere on the anterior vaginal wall If the ureters can be catheterized the diagnosis is made relatively easy In 2 cases only was the ectopic ureter catheterized and a pyelogram made

Cystoscopy with catheterization of the ureters may be of assistance although normal bladder and normal ureters are frequent findings The cystoscopies recorded all normal bladders with normal ureteral openings One might expect that an intravenous skiodan injection would be of value, but owing to the diminished function of these kidneys the secretion may be very slow and inadequate in amount to show an outline of the pelvis This was attempted twice in the author's case, but shadows other than those of the normal kidneys could be interpreted only in retrospect Plain X-rays of the kidneys are apparently not to be relied upon as the upper pole of the kidney lies high, and definite outlines are not obtained unless some means such as perirenal air injection be made The possibility of a vesico-vaginal fistula was ruled out by the usual method in the more recent cases Up to the present time a diagnosis of bilateral ectopic vaginal ureters has not been made before operation With the available equipment diagnosis should be made possible in childhood in all cases

TREATMENT

The need of correlating the surgical factors pertaining to the dispensation of this congenital lesion is well illustrated by the fact that twelve operative procedures were used in the treatment

of the 20 cases. Six patients were operated upon twice and 2 patients three times. Attempts to ligate the lower end of the ureter were unsuccessful. Death from extensive suppuration occurred in 2 cases when surgery was not applied. Neocystostomy was one of the first operative procedures used in an attempt to conserve the kidney. It was repeated in most cases and in one case it was followed by death and in another case by a recovery after a long illness. Complete nephrectomy was done in 4 cases with recovery. Both the kidneys were badly infected or the blood supply was so intricate that the upper kidney could not be removed without disturbing the vessels of the major kidney. Heminephrectomy was accomplished in 4 cases in which the kidneys were not infected and the blood supply was quite distinct from that of the larger kidney. Kummel and Graff report anastomosing the pelves on one side successfully.

Before any surgical procedure is applied, it should be borne in mind that (1) these kidneys have but little functional value, (2) that the ureter is most always dilated and (3) that these kidneys have a tendency to become infected. It is doubtful if a standardized operation can be devised to use in every case. Neocystostomy precludes infection. Once infection has taken place, a complete nephrectomy is indicated provided there is an opposite kidney. To leave a large cystic ureter in place would invite chances for infections. If the supernumerary kidney remains free from infection disposal of the supernumerary kidney and ureter should be brought about by surgery. When dilatation of the pelvis and ureter has not taken place the pelvic anastomosis of Kummel and Graff seems feasible provided the ureter be removed. When the supernumerary kidney and ureter are dilated and the kidney possesses distinct and separate vessels a heminephrectomy is the procedure of choice. But many of the supernumerary kidneys showed a very intricate blood supply and a hemine phrectomy could not be done without interference with the vessels of the good kidney. Such was the condition found in the author's case. Here a ureterectomy seemed to be the operation of choice. It was easy to accomplish and a complete conservation of the good kidney was maintained. The supernumerary kidney apparently atrophies as one would not expect any more complication than ligating a normal ureter. While this operation has not been corroborated, it offers good possibilities in cases in which the diagnosis has been made early before infection has taken place.

CONCLUSIONS

1. Ectopic vaginal ureters produce uniform symptoms of vaginal dripping of urine which exists with normal urinations.

2. The opening for ectopic vaginal ureter is on the anterior vaginal wall near the midline anywhere from the hymen to the cervix.

3. The right side is the more frequently involved.

4. The ectopic vaginal ureter always runs to the upper pole of the kidney.

5. The kidney attached to the ectopic vaginal ureter is of little functional value and is prone to infection.

6. Intravenous thiodan may not be of value in diagnosis of these cases.

7. No attempt should be made to conserve these ureters and kidneys.

8. Hemineprhrectomy may be done if vessels are distinct to each kidney.

9. Once infected, complete nephro-ureterectomy is indicated.

10. Diagnosis should be made in the first decade.

11. The operation, total ureterectomy, offers an easy method of treatment when infection has not taken place.

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THE CLINICAL MANAGEMENT OF INJURIES TO THE HEART AND PERICARDIUM

Report of Seven Cases[1]

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In the 2 year period between October, 1932 and October, 1934 there were admitted to the Louisville City Hospital 7 patients in whom injuries to the heart or pericardium were of major importance. The symptoms for the most part were those of increased intrapericardial pressure superimposed on those of primary or secondary shock. However when the blood escaped externally or into one or the other of the pleural cavities, the evidences of acute cardiac compression were intermittent or absent. In 2 cases cerebral symptoms were outstanding. Five of the patients required major surgical treatment.

From the standpoint of management these acutely wounded individuals may be classified as follows: (1) patients with definite intrapericardial hemorrhage who improve under observation and recover without exploration—Cases 1 and 2; (2) those in whom improvement is slow or in whom there is recurring elevation of intrapericardial pressure accompanied by increasing hemothorax, that require exploration—Cases 3 and 4; (3) patients with marked tamponade who require prompt operation—Cases 5 and 6; and (4) those with large wounds accompanied by alarming external or internal hemorrhage, in whom intervention is heroic and usually futile—Case 7.

Five of the patients recovered and 2 died. Their management, both from a medical and surgical standpoint, may be best critically evaluated by a study of the case records.

Case 1. A colored male, 24 years of age, admitted to hospital 2½ hours after being stabbed over the left precordium. Hemopericardium with spontaneous decompression into the left pleural cavity. Improvement and recovery under conservative treatment.

L. F. L.C.H. No. 21555, was admitted to the hospital, November 3, 1932, at 11:25 a.m., in severe shock, with numerous stab wounds of the body and arms. He was said to have been stabbed about 10:00 p.m. with a sharp, 6-inch knife. He became weak and dazed, and was brought to the hospital in a police patrol. Examination, aside from relatively minor lacerations of the arms and face, revealed one short, perforating wound in the left third interspace about 6.5 centimeters from the midsternal line and another just to the right of the xiphoid process. The pulse was weak and irregular. The respirations were rapid, and the patient complained of a sensation of smothering. The blood pressure was 80/30.

Treatment was instituted immediately to combat shock. A solution of 5 per cent glucose was administered intravenously. When he had received 1200 cubic centimeters, the blood pressure was 130/80. The infusion was discontinued. The wound in the epigastrium was explored under 1 per cent procaine hydrochloride anesthesia, and found not to enter the peritoneal cavity. He was given tetanus antitoxin, 1500 units, and put to bed. Three hours later the blood pressure was 80/60. Glucose was infused slowly for the next 3 hours. At 9:30 a.m., his pulse was strong and regular but he complained of moderate substernal discomfort. A portable roentgenogram showed a left mild hemothorax, with widening of the cardiac shadow consistent with hemopericardium. The dense shadow of the left border of the heart could be seen about 1 centimeter within the pericardial outline (Fig. 1). The course for the next few days was characterized by elevations of temperature, in part probably due to an infection in the epigastric wound. On November 6, a film showed a left mild hemothorax, but the cardiac shadow was normal in size and contour. On November 11, 300 cubic centimeters of bloody fluid, sterile on cultures, were aspirated from the left pleural cavity. On November 13, film showed an area of increased density in the lower left lung field with air in the adjacent costophrenic angle (Fig. 2). The patient was discharged against advice. Shortly afterward he returned to work as a street cleaner.

On March 2, 1934, 16 days after his injury, the patient returned for the repair of a left inguinal hernia. Examination revealed the heart and lungs to be normal in all essentials.

When seen in the follow-up clinic on April 12, 1935, he stated that he had been working regularly but for the past year he had had frequent dizzy spells accompanied by knife-like pains over the precordium. Examination showed no abnormality of the heart or lungs. The blood pressure was 120/80. A film of the chest was negative. An electrocardiogram was normal.

Case 2. A colored male, 35 years of age, admitted to the hospital shortly after being stabbed over the right precordium. Pneumohemopericardium. Conservative treatment. Uneventful recovery.

J. S. L.C.H. No. 38543, was admitted to the hospital, September 20, 1934, at 5:00 p.m., shortly after having been stabbed in the right chest with a pair of scissors. The wound penetrated the thorax in the third interspace just to the right of the sternum. It was sucking air. The patient was in very good condition. The pulse was of good quality, rate 80. The blood pressure was 115/70. Examination revealed a right pneumothorax, but nothing abnormal was observed concerning the heart. The external wound was sutured, and the patient was put to bed for observation. Pulse and blood pressure readings were recorded frequently. At 10:30 p.m., the blood pressure was 84/60. Crepitation of the soft tissues of the right chest wall, limited to the region of the wound, was noted. The cardiac dullness was found to be replaced by a tympanitic note, and the heart sounds, though easily heard, were muffled.

The electrocardiographic studies in all of the cases were made by Dr. J. Murray Kramer. The roentgenograms were made and interpreted under the direction of Dr. S. R. Johnson.

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Fig 1 Case 1 Eight and one half hours after admission Roentgenogram (portable) made with the patient in the semirecumbent position Hemopericardium and hemothorax left The denser shadow of the left border of the heart may be seen medial to the outline of the pericardium

with a peculiar, slushing second sound which was loudest over the base The rhythm was regular A film of the chest made on admission showed a right sided pneumothorax with a pneumohemopericardium (Fig 3)

At 9.00 a m , the following morning, the tympany over the precordium and the slushing sound had disappeared A film then showed a definite enlargement of the cardiac shadow which involved chiefly the area of the left ventricle, but no air was visible in the pericardium There was moderate emphysema of the right chest wall (Fig 4) The blood pressure reading was 100/60 The pressure in a cubital vein was 15 centimeters of water On September 24 an electrocardiogram showed slurring of the *QRS* complexes in lead 1 only, and inversion of the *T* waves in leads 2 and 3, which was very suggestive of the coronary (Pardee) type and indicated coronary damage On October 4, a film showed both lung fields practically clear, except for slight increase in density in the right costophrenic angle (Fig 5) He was discharged on October 7, in satisfactory condition and did not return to the follow up clinic

These 2 cases exemplify recovery without operation The diagnosis in the first case depended upon the clinical and X-ray evidence of blood within the pericardial cavity, in the second case, upon the evidence of blood and air Management, in both instances, consisted of, first, combating shock and, second, careful observation Thoracocentesis of the left pleural cavity, in Case 1, was carried out after the danger of secondary hemorrhage had passed

Fig 2 Case 1 On discharge from the hospital Film made at 6 feet, 2 days after thoracentesis The heart shadow has returned to normal size There is an area of increased density in the lower left lung field with air in the adjacent costophrenic angle and elevation of the diaphragm

Case 3 A colored male, 40 years of age, with an icepick wound of the left chest and a contusion of the left frontoparietal region Signs and symptoms of acute cardiac compression, overshadowed by evidences of a left cerebral lesion, confused observers and delayed operative intervention Exploratory thoracotomy with pericardial decompression 18 hours after admission Death 24 hours later from prolonged cerebral anoxemia with terminal pulmonary edema

W M , L C H No 28283, was admitted to the hospital, August 4 1933 at 8.45 p m , following a fight in which he had received a contusion of the left frontoparietal region and an icepick wound of the left chest, sixth interspace, midaxillary line He was under the influence of alcohol and in shock He was moderately dyspneic, restless, and complained of thirst The pupils were equal, regular, and reacted to light and accommodation The radial pulse was very feeble and difficult to palpate The blood pressure could not be obtained The heart sounds were distant and of poor quality, but the rhythm was regular There was no increase in the area of cardiac dullness Auscultation revealed a few râles in the region of the wound The patient failed to respond to immediate conservative treatment and lapsed into a state of stupor A right facial paralysis was observed and this gradually extended to a complete right hemiplegia These findings, in the presence of a contusion of the scalp, were misinterpreted as indicative of direct injury to the cerebrum

The following morning, at 11 30 a m , he was still stuporous The pulse was imperceptible It had never been slow and bounding as it is as a rule with increased

Fig. 3 Case 1. On admission Roentgenogram made at 6 feet showing pneumohemopericardium and pneumothorax, right

Fig. 4 Case Sixteen hours after admission Roentgenogram (portable) made with the patient in the semi recumbent position Air is no longer visible in the pericardial sac. Note that the enlargement of the cardiac shadow due to hemopericardium involves chiefly the region of the left ventricle There is fluid level at the right base and emphysema of the chest wall

intracranial pressure It had not been possible to record the extremely low blood pressure The respirations were short and gasping, of the air-hunger type The pupils were equal and reacted to light Examination of the cranial nerves revealed that the third, fourth, and sixth were normal, the corneal reflex was diminished (fifth) the right lower segment of the face was almost completely paralyzed (seventh) and the remainder were normal. There was a right hemianesthesia to pin prick of the body and extremities and right hemiplegia with absent deep reflexes A spinal puncture revealed clear fluid, under a pressure of 400 millimeters and with normal mechanics X-ray films of the skull were negative for fracture A roentgenogram showed a large cardiac shadow very wide in the upper portion and overshadowing the aortic knob A large, distended vena cava was visible The increased intracranial pressure was now interpreted to be secondary to the increased venous pressure and the coma and neurological changes were for the first time recognized to be due to secondary cerebral anoxemia A diagnosis of hemopericardium with tamponade was made

Operation was performed 8 hours after admission, by Dr R. A Growald His operative note follows "Under local per cent procaine hydrochloride anesthesia, Spangaro incision was scratched out with the horizontal limb over the fourth rib One inch of the left fourth costal cartilage was resected exposing the pericardium without opening the pleura The pericardium was tense, blue, and feeble transmitted pulsation was visible The incision was continued, resecting about 4 inches of the fourth costal cartilage and rib and the pleura was opened widely under increased pressure of oxygen transmitted through a closely fitting anesthetic mask and a rebreathing bag The pericardium was opened and 600 cubic centimeters of blood under great pressure gushed out The heart beat, which had been feeble, increased in amplitude and strength A blood pressure of 100 systolic was obtained immediately and the temporal pulse could be felt for the first time A traction suture of silk was placed in the apex, and the heart was drawn as far as possible out of the wound A second suture was placed in the wall of the left ventricle, and the heart was rotated about 90 degrees to the right No bleeding into the pericardial sac was seen, and the wound of the heart was too far posterior to be visualized The pericardium was closed loosely leaving an opening 1 inch in diameter communicating with the left pleural cavity One rubber tissue drain was placed down to this opening, and the wound was closed in layers with silk. The air in the pleural cavity was forced out by increased pressure of oxygen during closure

The condition of the patient was fair at the end of the operation. A spinal puncture then revealed fluid pressure of 80 millimeters He was returned to bed and placed in an oxygen tent, but the change of the pulse and the blood pressure declined rapidly and consciousness never returned The temperature continued to rise Death occurred 24 hours later apparently due to prolonged cerebral anoxemia and terminal pulmonary edema

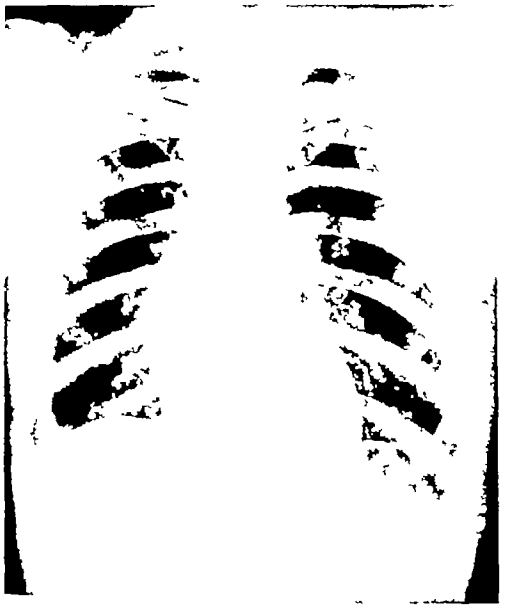

Fig 5 Case 2 On discharge from the hospital Film made at 6 feet The contour of the heart is normal There is an area of increased density in the right costophrenic angle.

Fig 6 Case 4 Thirteen and one-half months after injury The lateral arm of the incision was placed over the fifth interspace and extended out to the stab wound at the anterior axillary line The face is symmetrical and there is no atrophy of the right arm He complains of weakness of the hand

A postmortem examination showed an icepick wound in the posterior wall of the left ventricle with a laceration of a coronary vein There was no fresh blood in the pericardial sac, but the left pleural cavity contained about 500 cubic centimeters of sanguineous fluid The lower lobe of the left lung was atelectatic. The remaining lobes of both lungs were edematous The skull showed no fracture, and the brain appeared normal There were a few recent infarcts in both kidneys

CASE 4. A colored male, 38 years of age, stabbed in the left fifth interspace, anterior axillary line Signs and symptoms of intermittent acute cardiac compression associated with evidences of cerebral anoxemia Suture of laceration of left ventricle 10 hours after admission Recovery complicated by right sided hemiplegia and motor aphasia.

V H, L C H No 34195, was admitted, March 25, 1934, at 3.45 a m., about an hour after having been stabbed in the left chest. Though he was brought to the ward in a wheel chair and was able to climb on the examining table, he was found to be pulseless There was a stab wound an inch long in the left fifth interspace at the anterior axillary line. The blood pressure could not be obtained He was under the influence of alcohol, and a good portion of his findings were attributed, at first, to that condition The veins of the neck and arms were distended Auscultation revealed very distant heart sounds A portable film of the chest showed widening of the cardiac and upper mediastinal shadows. There was increased density throughout the entire left lung field Five per cent glucose solution was introduced intravenously Frequent pulse and blood pressure readings were taken At 10.45 a m , the blood pressure was 90/50, but shortly afterward no reading could be obtained When seen at noon he was stuporous The body was very rigid, and there was constant twitching of the right side of the mouth Auscultation revealed distant heart sounds of a very poor quality The pulse was paradoxical The blood pressure as recorded on the chart of the previous 2 hours showed fluctuation At 12 55 p m , the patient was sent to the operating room There a blood pressure reading of 140/80 was obtained The heart sounds were easily heard and the pulse was bounding The peripheral venous dilatation had diminished The facial twitchings persisted, however Evidently the pericardial sac had decompressed itself into the left pleural cavity, but, in view of the observations of the morning, exploration was carried out by the writer, 10 hours after admission

Under local 1 per cent procaine hydrochloride anesthesia a Spangaro type of incision was scratched out, with the horizontal limb over the left fifth interspace The sternal portion was deepened, and 1 5 centimeters of the sixth costal cartilage were resected The internal mammary artery was ligated The transverse thoracic muscle was separated in line with its fibers, and the pleura was dissected free from the distended, dark-colored pericardium The pericardium was incised and blood spurted out under pressure In order to prevent further hemorrhage a clamp was used to close the opening in the pericardium while wider exposure was obtained Three centimeters of the fifth costal cartilage were resected Nitrous oxide-oxygen anesthesia under positive pressure was begun, and the horizontal limb of the incision was deepened into the left pleural cavity A laminectomy retractor inserted through the fifth interspace provided beautiful exposure of the pericardium and the lung The pleural cavity was packed off with moist gauze and the pericardium was opened

Fig. 7. Case 5. On admission. Roentgenogram (portable) showing enlargement of cardiac shadow. Hemopericardium found at operation.

Fig. 8. Case 5. Two and one half months after injury. Film made at 6 feet. The heart heart ratio is [illegible] centimeters [illegible] centimeters. The cardiac lesion is stenosis of rheumatic heart disease.

on its long axis. After reduction of the intrapericardial pressure the heart action improved remarkably, the blood pressure increased immediately to 70/[illegible]. The remaining blood and many clots were aspirated. A laceration an inch long was observed in the left wall of the pericardium. A traction suture of silk was placed through the apex and the heart was drawn out of the wound for inspection. On the posterior lateral wall of the left ventricle was a small laceration about one fourth inch long through which blood oozed with each systole. No attempt was made to determine whether or not the wound penetrated into the cavity of the heart. Three interrupted silk sutures were used to control all hemorrhage. The edges of the pericardium were approximated with single suture loops using a simple drainage for decompression into the left pleural cavity. No injury to the left lung was observed although the knife must have passed through it. Under positive pressure maintained through tightly fitting mask the lung was re-expanded and the wound closed carefully in layers without drainage, interrupted catgut sutures being used. A sheet of gutta percha was placed over the wound, to act as a shield, should there be any tendency toward leakage of air into the chest. The blood pressure was now 100/100. The patient was placed in bed under an oxygen tent.

For the next 3 hours, the blood pressure fluctuated between 80 and 90. The pulse remained of good quality. [illegible] shortly after the close of the operation [illegible] cubic centimeters of blood was aspirated from the left pleural cavity. [illegible] was given [illegible] cubic centimeters of citrated blood intravenously. The following morning his condition was good but he was still in stupor. Weakness of the right side of the face and body was evident. The temperature was [illegible] degrees F., the blood pressure [illegible]. Another transfusion of [illegible] cubic centimeters of citrated blood was given.

On March 17 he was no longer stuporous, but remained confused and motor paresis was noted. Complete right hemiplegia with hemianesthesia persisted. The pupils remained equal and reacted to light. A spinal puncture revealed clear fluid under a pressure of [illegible] millimeters and normal mechanics. The fluid contained no cells and no blood was present, and the Wassermann reaction was negative. The temperature was [illegible] degrees F. Seventy five cubic centimeters of bloody fluid serum or serum was aspirated from the left pleural cavity. On March [illegible] he moved the right leg. A spinal puncture revealed clear fluid under pressure of [illegible] millimeters. On March 20 [illegible] heart still showed for travel slow [illegible] throughout the entire left lung field and considerable pleural markings throughout the right lung which were consistent with hemorrhagic infarcts. Comparison with the [illegible] made before operation showed that, after correcting for distortion, the transverse diameter of the heart shadow [illegible] from 16 centimeters to [illegible] centimeters. By April [illegible] temperature was normal. The wound was healed [illegible] the stitches were removed. From this day on there was

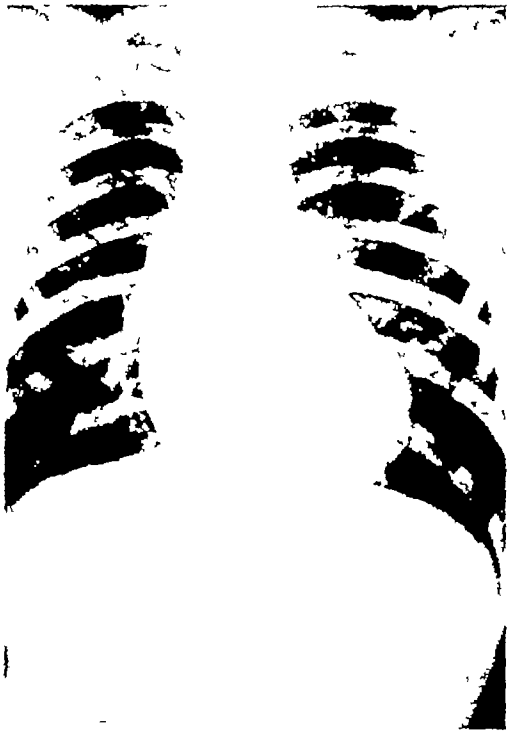

Fig 9 Case 5 One year after injury Film made at 6 feet. The heart-chest ratio is 13 centimeters to 25 5 centimeters Comparison with Figure 8 indicates an advancing cardiac lesion the nature of which is not clear

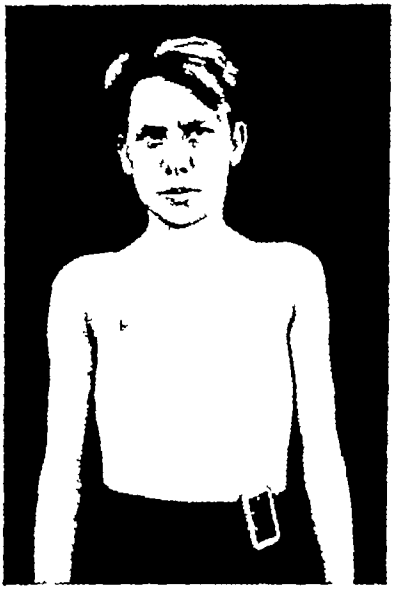

Fig 10 Case 5 Thirteen and one half months after injury Because of suspected injury to the right internal mammary artery the vertical arm of the incision was placed over the artery Exposure of the right ventricle caused an inconsequential defect in the sternum

gradual return of the sensory and motor functions of the right side of the body Transitory states of confusion and motor aphasia persisted until the fourth postoperative week. On April 3, a roentgenogram showed clear lung fields and the contour of the heart was normal On April 10 an electrocardiogram showed slurring of the *QRS* complexes in all three leads, inversion of the *T* wave in lead *2* and left axis deviation There was no evidence of fixation of the heart as determined by shifting the position On the day of discharge, May 6 1934, 42 days after injury, he seemed mentally alert, but there was residual weakness and clumsiness in the right arm and hand Neurological examination showed no appreciable abnormalities otherwise

When seen in the follow up clinic on April 11, 1935, the patient stated that about a month after discharge he had returned to his work in an axe handle factory and had continued to work up to the present time The right arm and hand were still weak. He had not been troubled by precordial pain, dyspnea, or edema Examination of the heart and lungs revealed no abnormalities The blood pressure was 130/80 A film of the chest appeared normal An electrocardiogram showed an upright *T* wave in lead *2* This had been inverted previously There was no evidence of fixation of the heart. On May 15, a roentgen kymogram was interpreted as normal Figure 6 is a recent photograph

In Cases 3 and 4 the cerebral symptoms were striking The disastrous pre-operative delay in Case 3 resulted from the failure to recognize persistent cerebral anoxemia due to cardiac compression As a result of this experience, the rigidity of the body and the twitchings of the face in Case 4 were interpreted correctly, and operation was carried out early enough to prevent permanent cerebral damage The effects of prolonged cerebral anoxemia are well known In 1922, Cannon and Cattell pointed out that as a result of low arterial blood pressure, functional and morphological damage to the central nervous system occurs In 1924, Cutler, Levine, and Beck in experiments in which the aorta and pulmonary artery were constricted temporarily in cats, observed that even though the heart might recover its normal rhythm following an obstruction of more than 3 minutes, the animals were left in a peculiar decerebrate state and died within a few hours or after a few days exhibiting marked opisthotonos accompanied by muscular rigidity and twitchings In the experiments cited the cerebral symptoms were always bilateral, whereas in Cases 3 and 4 the evidence pointed to damage in the left cerebral cortex No explanation of this unilaterality seems entirely satisfactory The possibility of pre-existing vascular disease on the left, or of localized arterial spasm, made manifest by the insult of anoxemia, might be mentioned Again, the question of embolism should be raised

Fig. 1. Case 6. On admission. Roentgenogram (portable) showing enlargement of the cardiac shadow confined to the left half. Tamponade due to extrinsic pressure by an extrapericardial hematoma.

Fig. 2. Case 6. Seven and one half months after injury. The scar of the stab wound can be seen medial to the areola.

since in both cases there was an injury to the left ventricle of the heart with the possible formation of mural thrombi. In Case 3 fresh infarcts in the kidneys, perhaps the result of emboli, were present. The brain was normal macroscopically. No microscopic studies were made. The recovery in Case 4, while relatively slow, resulted in practically complete restoration of function.

Case 5. A white boy, years old, admitted with a gunshot wound of the right precordium. Unmistakable cardiac tamponade. Operation hour and 5 minutes after admission. Suture of laceration of right ventricle. Complete clinical recovery complicated by pertussis. Electrocardiogram showed evidence of coronary damage.

W. C. L. C. H. No. 34388, was admitted, March 31, 1934, at 5.30 p.m., shortly after having received a .22 caliber rifle wound of the right chest. The point of entrance was at the junction of the fourth costal cartilage with the sternum. There was no point of exit. The patient was in severe shock, sweating, and very restless. No blood pressure reading or pulse could be obtained. The veins of the neck were distended. There was no increase in the area of cardiac dullness. The heart sounds were distant and weak. A portable roentgenogram showed definite enlargement of the cardiac shadow (Fig. 7). Anteroposterior and lateral films of the abdomen showed the bullet at the right anterior margin of the twelfth thoracic vertebra. The body of the vertebra had been slightly damaged by the bullet. There was no free air in the peritoneal cavity. Intravenous glucose and acacia were administered, but the condition of the patient did not improve satisfactorily.

Operation was performed by the writer hour and 5 minutes after admission. At this time the blood pressure was 80/40. Nitrous oxide oxygen anesthesia under slightly positive pressure through tightly fitting mask was used. A vertical incision with excision of the bullet hole was made just to the right of the sternum, exposing the second to sixth costal cartilages. The fourth and fifth cartilages were resected disclosing a laceration of the right internal mammary artery. The artery was doubly ligated with silk and divided. The right pleural cavity was opened while stripping the pleura from the pericardium, and was left open. An aspirating needle, introduced into the intact pericardial sac revealed blood. The sternum was completely cut across at the level of the fourth interspace and a triangular portion of the lower segment was resected. Very Care was taken to preserve the attachments of the cartilages on the left. The pericardium was opened as far as long as on the right anterior surface. About a double handful of clots rolled out. The heart action immediately improved and the blood pressure rose to 140/80. There was a wound which bled freely on the upper anterolateral wall of the right ventricle. It appeared as though a bullet had been taken out of the periphery of the cardiac muscle with dull instrument. A tracion suture of silk was placed through the lower portion of the ventricle, and two silk sutures were placed through the laceration successfully controlling the hemorrhage. The pericardial cavity was irrigated with warm saline, freed of all clots, and observed for further oozing. As far as could be determined there was no other wound in the heart. The point of exit from the pericardial cavity was observed over the dome of the liver. It was now seen that distal to the sutured wound the cardiac muscle had turned purplish in color. Fearing that an important vessel had been heated, the sutures were removed. This was followed by rather profuse hemorrhage. The sutures were replaced, this time more superficially. Hemorrhage was more difficult to control with the shallower

Fig 13 Case 6 Six and one-half months after injury Film made at 6 feet. Notice the elevation and rounding of the apex and the loss of definition suggestive of intrapericardial adhesions in this region.

Fig 14 Case 6 Seven and one-half months after injury Compare with Figure 13 Roentgen kymogram showing inactivity (dot) interpreted as definite evidence of localized intrapericardial adhesions

bites, and four sutures were necessary to stop it completely Satisfied that the circulation in the heart muscle was now unimpaired, the wound was closed in layers with interrupted silk sutures under positive pressure No drain was used but the pericardium was left open to decompress itself into the right pleural cavity A sheet of gutta percha was placed over the wound, to act as a valve, should there be any tendency toward leakage of air into the chest The patient was returned to bed and placed under an oxygen tent The blood pressure reading was now 130/80

His convalescence was relatively stormy On April 1, the first postoperative day, he was given 150 cubic centimeters of citrated blood The blood pressure stabilized around 100/70 On April 2, he was restless, complained of the dressing, and tore it off The wound was not harmed A portable roentgenogram showed marked widening of the cardiac shadow, and cloudiness and soft mottling throughout both lung fields consistent with bronchopneumonia His temperature was 101 degrees F On April 5, the chest had cleared, and the oxygen therapy was discontinued On April 10, the ninth postoperative day, the wound was clean and the stitches were removed A film of the chest showed the heart shadow as previously described, but the lung fields were clear He began to cough By April 18 he had a frank case of pertussis and was transferred to the isolation ward where he withstood the paroxysms of coughing and recovered without further complications On April 30 an electrocardiogram showed slurring of the *QRS* complexes in all leads and low voltage There was no evidence of fixation of the heart on shift of position He was discharged on May 8, 1934, 38 days after his injury

On June 15, 1934, the patient was readmitted He stated that he had had several attacks of pain which originated under the left scapula and radiated to the precordium, and that they would last for an hour or so He had been dyspneic on exertion The cough had persisted, but he had not suffered with a sore throat or joint pains Examination revealed a pulsating precordium (operative defect in the sternum) but the heart and lungs otherwise seemed normal The blood pressure was 106/75 The pulse rate was 122 the temperature, 99 4 degrees F On June 16 an X-ray film of the chest made at 6 feet showed the heart-chest ratio to be 11 centimeters to 22 centimeters As compared with previous films the heart shadow was definitely smaller (Fig 8) On June 18, an electrocardiogram was normal, the voltage was no longer low There was no fixation of the heart The temperature became normal on the third day, and he was discharged on June 23, greatly improved

On September 8 1934 he was readmitted because of conjunctivitis secondary to an abrasion of the cornea of the left eye He had no complaints referable to the heart Examination showed no abnormalities of the heart or lungs

When seen in the follow up clinic on April 12, 1935, he stated that he had no pain in the chest, but occasionally

suffered with soreness localized over the region of the twelfth thoracic vertebra. He could run and play without pain or dyspnea. Examination of the chest revealed the sternal defect with the transmitted pulsations, but the heart and lungs were negative in all essentials. The pulse was regular and of good volume. The blood pressure was 108/70. A roentgenogram made at 6 feet showed moderate transverse enlargement of the heart with heart chest ratio of 3 centimeters to 25.5 centimeters. The right border of the heart was about 5 centimeters from the mid line. The contour was not unlike that seen in rheumatic heart disease (Fig. 9). An electrocardiogram showed a deep Q_3, 7 millimeters in amplitude which was 70 per cent of the greatest R wave in any lead, indicating coronary damage. There was no fixation of the heart. On 3/1/3[illegible], a roentgen kymogram showed variation in the shape of the w[illegible] in the region of the left and right auricles, but there was no evidence of fixation of the heart to the pericardium. A recent photograph is shown in Figure 10. The bullet has not been removed and it is likely that this will never be necessary.

There are several features of this case that are interesting. (1) The clinical signs of acute cardiac compression, embracing the triad stressed by Beck(1) were present. This triad is characterized by (a) a low arterial pressure, (b) a high venous pressure, and (c) a small, quiet heart. (2) The exposure of the heart was unorthodox, but particularly satisfactory. In this case injury to the right internal mammary artery was anticipated, and the perpendicular incision was placed directly over it. Resection of the fourth and fifth costal cartilages afterward cutting across the sternum and rongeuring away a triangular portion of the lower segment, provided satisfactory exposure of the wound in the heart and left an inconsequential defect. (3) The deep sutures which at first were inserted in the heart had to be replaced by more superficial sutures in order to avoid the possibility of circulatory embarrassment to the myocardium peripheral to them. (4) Pertussis, after operation was an unexpected complication, however it seemed to have no harmful effect on the chest wall or heart. (5) Comparison of the electrocardiograms is of special interest: the first one, made 1 month after injury while the patient was convalescing from pertussis, showed only low voltage; the second one, recorded 6 weeks later, was normal; while a recent tracing, a year after injury, shows evidence of coronary damage. One may conjecture as to the relationship between the delayed coronary damage and the change in the color of the heart muscle following the placing of the sutures. It is difficult to account for the persistently abnormal contour of the heart as seen in the X ray films on the basis of an injury to the right ventricle. This contour on the other hand appears to be characteristic of rheumatic heart disease. As is well known, X ray evidence of rheumatic heart disease is observed frequently in the absence of a clear history or definite clinical signs of the disorder. The deep Q_3 seen in the recent electrocardiogram may be observed in rare instances in rheumatic heart disease. Additional electrocardiograms and roentgenograms should be made in this case over a period of years.

CASE 6. A colored female, 43 years of age, admitted with stab wound over the left precordium. Acute cardiac compression due to an extrapericardial, mediastinal hematoma disclosed at operation 2½ hours after admission. Uneventful recovery. Roentgenologic evidence of localized intrapericardial adhesions.

H.T. L.C.H. X 26700, admitted, September 17, 1934, at 8:35 p.m. shortly after receiving several stab wounds of the body. All were minor except one that penetrated the thorax 8 centimeters to the left of the midsternal line in the fourth interspace. There was no considerable loss of blood externally. She was under the influence of alcohol and in shock. The pulse and blood pressure could not be obtained. The area of cardiac dullness was thought to be increased, and the heart sounds were distant. The veins of the neck were distended. A venous pressure reading of 4 centimeters of water was obtained. There was no hemothorax or pneumothorax. A portable film of the chest showed enlargement of the cardiac shadow which was greatest on the left side (Fig. [illegible]). One hour later, following intravenous shock therapy with 5 per cent glucose, a blood pressure reading of 64/38 was obtained. A diagnosis of pericardial injury with tamponade was made.

Operation was performed by the writer 1 [illegible] hours after admission. The blood pressure at the beginning of the procedure was 80/50. The pulse rate was 70. Nitrous oxide-oxygen anesthesia was used under slightly positive pressure through a snugly fitting mask. A Sprengure type of incision was marked off with the horizontal arm swinging around the left chest wall beneath the breast. The sternum was dissected down to the ribs and intercostal muscles, and the left breast and pectoralis major muscle were reflected upward to expose the fourth interspace. There was a perforation about 3 centimeters from the sternum through which blood spurted with each expiration. The third and fourth costal cartilages were resected, and lacerated internal mammary artery was found to be bleeding freely. It was ligated with silk. A dark colored tumor mass, which we took to be a distended pericardium, protruded into the wound. To our surprise on attempting to open it, [illegible] found it to be large hematoma which had dissected downward between the left pleura and the pericardium laterally and into the mediastinal tissues anteriorly and to the right. Following exposure of the hematoma the blood pressure rose immediately to 90/40 and remained at that level throughout the rest of the procedure, indicating that the heart had suffered from compression which was in this case extrapericardial in origin. There was only a very small amount of blood within the pericardial cavity. A traction suture of silk was placed in the apex and the wall of the heart was carefully inspected. No injury was found. Unfortunately troublesome bleeding from the myocardium occurred when the traction suture was removed. This required several sutures to control it. Feeling satisfied that all hemorrhage had been stopped, the anesthetist increased the positive pressure and I closed the wound tightly in layers with interrupted silk sutures. No drain was used, but the pericardium was left open for decompression through a communication with the left pleural cavity. A sheet of gutta percha was placed over the

wound, to act as a valve, should there be any tendency toward leakage of air into the chest. The patient was returned to bed in very good condition with a blood pressure of 140/80 The venous pressure immediately after the operation registered 10 centimeters of water

The patient improved progressively The temperature was never above 99 degrees F The blood pressure remained within normal limits. The wound healed cleanly, and the stitches were removed on the eighth day On October 15, the eighteenth postoperative day, an electro cardiogram showed no change in the *QRS* complexes with the exception of a Q_3 which was less than 25 per cent of the amplitude of the greatest *R* wave, there was inversion of the *T* waves in leads *1* and *2*, fairly characteristic of the coronary (Pardee) type. There was no evidence of fixation of the heart to the chest wall. On October 17, a roentgenogram showed a heart shadow of normal size with haziness of contour in the region of the apex suggestive of intrapericardial adhesions. There was moderately increased density in the lower half of the left lung field She was discharged on October 21, 1934, 24 days after her injury

When seen in the follow up clinic on April 12, 1935, she had no complaints and had been doing her house-work. Aside from a keloid scar (Fig 12), the examination of the chest was negative. The blood pressure was 108/70 A film of the chest made at 6 feet showed the right border of the heart to be normal, but, as had been noted in the film of October 17, 1934, there was elevation and rounding of the apex with loss of definition suggestive of intrapericardial adhesions in this region. The heart-chest ratio was 12 5 centimeters to 25 centimeters (Fig 13) An electrocardiogram showed the *T* wave of leads *1* and *2* to have changed from the fairly deep inversion shown previously to flat waves with just a suggestion of elevation. Lead *3* showed the Q_3 previously seen, but it was without essential alterations otherwise. There was no evidence of fixation of the heart to the chest wall. The changes were interpreted to indicate that the coronary damage had not progressed, but on the contrary probably had improved On May 15, a roentgen kymogram (Fig 14) verified the diagnosis of intrapericardial adhesions in the region of the apex as had been suggested by the films of October 17, 1934 and April 12, 1935

This case is interesting in that the acute cardiac compression was due to pressure exerted from outside the pericardium A laceration of the left internal mammary artery had resulted in the formation of a mediastinal hematoma Immediate improvement followed its exposure The follow-up X-ray films indicate the formation of intrapericardial adhesions in the apical region This is the only case in which intrapericardial fibrosis has been observed and the complication has caused no symptoms As in Cases 4 and 5, no drain was used The pericardial cavity was left open to communicate with the pleural cavity for decompression and drainage

CASE 7 A colored male, aged 22, operated upon 30 minutes after a stab in the left chest. Large laceration of left ventricle, 3 liters of blood in left pleural cavity Death on table.

J.D, L.C.H. No 29433, was seen on August 20, 1933, in the accident ward 10 minutes after having been stabbed in the left third interspace, anterior axillary line. The respirations were labored, short, and gasping The pulse was rapid and thready The patient was unconscious. He was rushed at once to the operating room

The operation was performed by Dr R. A. Griswold. His operative note follows "The patient was prepared rapidly, and a left Spangaro incision was made without anesthesia. The left pleural cavity contained about 3000 cubic centimeters of blood There was a stab wound through the left lung and pericardium extending into the upper portion of the left ventricle. The cardiac wound was L-shaped and measured about 1 by 1 5 inches It was spurting blood. A traction suture was placed in the apex, and the cardiac wound was closed with interrupted silk sutures. Artificial respiration, and intravenous glucose and acacia had meanwhile been given Spontaneous respiration did not occur The heart beat gradually became weaker and, despite massage and the intracardiac injection of adrenalin, its contractions ceased Death occurred not from tamponade, but from hemorrhage into the pleural cavity "

Permission for a postmortem examination was not obtained

Operation on this patient was heroic, but it is conceivable that he might have been saved In another such instance an autotransfusion, utilizing the large amount of blood in the pleural cavity, would be given immediately on the table

OBSERVATIONS ON CLINICAL MANAGEMENT

Because wounds may occur in deep seated organs which are far from the point of apparent injury, it is our practice to observe all patients with wounds of the chest and upper abdomen over a considerable period of time in order to rule out injury to the heart or pericardium In patients with wounds over the precordium, in whom pericardial or cardiac injury is more likely, every attempt is made to establish a correct diagnosis as soon as possible Diagnosis of pericardial or cardiac injury is not always easy. In this hospital, since the patients that are admitted are first seen by the senior interne, an attempt has been made to make all of the house-officers "heart-conscious" so that the very earliest signs will be recognized and valuable time will not be wasted Venous pressure determinations by the direct method outlined by Beck (3) are of special value in obscure cases In those patients admitted in shock, which often is far out of proportion to the apparent injury, and in whom the signs of Beck's triad, referred to in the comment under Case 5, are positive, a definite diagnosis is established immediately In others in whom there is evidence of moderately increased intrapericardial pressure, which may or may not be intermittent, the clinical and X-ray demonstration of blood (or, in rare instances air, Case 2) within the pericardial sac confirms the diagnosis In still others there may be very little evidence of increased intrapericardial pressure, but definite and progressive hemorrhage is occurring into one or the

other of the pleural cavities. Under these circumstances the blood may be coming from the heart, the great vessels or the lung and even though a definite diagnosis cannot be made exploration is indicated if the loss of blood is great.

Immediate treatment is directed against shock. The patient is placed in the Trendelenburg position, unless the depression of the head and thorax increases respiratory embarrassment. External heat is applied. Morphine is given in large enough doses to relieve pain and insure rest. If the degree of shock is great, 5 per cent glucose solution is administered intravenously. Pulse and blood pressure readings are recorded at 15 to 30 minute intervals, and the patient is carefully observed. In the meantime, relatives and friends of the patient are cross-matched for a transfusion. If no compatible donor is at hand, and it seems likely that a transfusion will be of sufficient benefit, a professional donor is secured by the institution. In a great emergency if blood cannot be obtained, 6 per cent acacia in 5 per cent glucose solution is used. Portable X-ray films of the chest are usually secured, but valuable time is not wasted in obtaining them if immediate surgical treatment is indicated by the clinical examination.

No definite time limit for the period of observation can be established. Each case must be considered individually and the response to the above plan of treatment is our guide to the course to be followed. If the response indicates probable recovery without operation, the wounds are subjected to débridement on the ward, and the patient is put to bed for further observation. On the other hand, if improvement is slow or there is evidence of recurring elevation of intrapericardial pressure accompanied by intrathoracic hemorrhage, preparation is made for exploratory thoracotomy. Patients with tamponade or alarming hemorrhage are prepared for operation at once. Morphine and atropine are given subcutaneously, the chest wall is shaved and the patient is transferred to the operating room. In the most urgent cases the patient is sent directly to the operating room where the preliminary medication and shaving are quickly attended to. The operative field is prepared with soap and water, ether and 70 per cent alcohol. Preparation is always made for the administration of intravenous glucose, and a transfusion or autotransfusion on the table, if indicated.

Anesthesia. Unless the patient is moribund there is no indication for operation without anesthesia. Pericardial exploration under local anesthesia as carried out in Cases 3 and 4 is so simple that it should be resorted to whenever the diagnosis is obscure. The operator should be prepared, however, to proceed with wide exposure of the heart without waste of time if the pericardium is found to contain blood. This has been emphasized previously by Bigger. For the additional exposure, which preferably opens the pleural cavity, inhalation anesthesia under slightly positive pressure through a rebreathing bag and a tightly fitting rubber mask is to be preferred. Should positive pressure equipment not be at hand an extrapleural approach may be used, however local or general anesthesia without positive pressure may be utilized for a transpleural approach in robust individuals, and, as will be seen, the advantages of internal drainage into the pleural cavity are great. If the pleura is opened and the chest wall is closed tightly without the expansion of the lung under positive pressure, the air may be aspirated from the pleural cavity immediately after tight closure. Occasionally the air may be left in the pleural cavity to help compress a lacerated lung which has not been sutured, and which might bleed again if the normal intrathoracic pressure relations were restored.

Operation. For exposure of the heart, as a rule, we have favored a modification of the intercostochondral thoracotomy of Spangaro, placing the horizontal arm of the incision over the interspace in which the wound is located. The use of the traction suture described by Beck (1) facilitates manipulation and the careful inspection and suturing of the heart. Silk is preferred to other suture materials. As already pointed out, no drains were used in Cases 4, 5 and 6. The pericardial cavity was left open to communicate with the pleural cavity for decompression and drainage. The relatively smooth convalescence of these patients leads us to favor this method. It is felt that there are several important objections to the use of drains: first, drains are irritating and increase the amount of pericardial effusion; second, they invite infection; third, they predispose to "sucking" in the wound and therefore to dangerous fluctuations in the pleural pressure; and fourth, they increase the possibility of intrapericardial fibrosis, no matter whether infection occurs or not. Closure of the chest wall is accomplished by continuous and interrupted silk or catgut sutures placed in such a way as to provide several

[illegible]

layers of closely approximated pleura, muscle, fascia, and skin It is often possible to stagger the layers slightly, in this way increasing the solidity of the closure Further to insure a tight chest wall, it is our practice to place a sheet of gutta percha or rubber tissue immediately over the wound This serves as a valve to prevent the entrance of air between the sutures in case approximation has not been sufficiently accurate

Postoperative care In general, the after care of the patient with the traumatic heart and pericardial condition does not differ from that following other major thoracic operations In the immediate postoperative period, frequent pulse and blood pressure studies are essential Special nursing care is a necessity An oxygen tent is not always required, but is of value when needed, particularly immediately after operation, or when late pulmonary complications occur We have employed routinely carbon dioxide and oxygen inhalations (10 per cent and 90 per cent) at frequent intervals and believe it has been of value in the prevention of atelectasis Higher concentrations of carbon dioxide may be used (7) Sanguineous fluid occasionally accumulates in fairly large amounts in the pleural cavity This may be removed by thoracentesis Should signs of cardiac tamponade occur after operation aspiration through the wound could be carried out, but this has not been necessary in any of our cases. Postoperative transfusions are of value and were used in 2 of 5 cases in this group X-ray films of the chest are probably needed more in the postoperative than in the pre-operative period, and are frequently of help in evaluating progress Satisfactory fluid intake is maintained by parenteral injections of normal saline or 5 per cent glucose solutions Diet is no different than that provided after other major surgical operations Morphine is given in adequate doses to insure relief of pain from the incision, and to keep the patient quiet. The usual principles of physiotherapy were employed in Case 4 to encourage and restore function in the paralyzed muscles All patients in this group received a prophylactic dose of tetanus antitoxin

Complications and sequelæ No instance of postoperative tamponade occurred Hemothorax was not troublesome, and no patients developed empyema The wounds healed without infection Cerebral symptoms occurred in 2 cases and resulted in death in 1 (Case 3), but only slight residual weakness in the right arm and hand in the other (Case 4) Mild bronchopneumonia with early recovery complicated Cases 4 and 5 Pertussis in Case 5, which appeared on the seventeenth postoperative day, did not cause additional sequelæ The X-ray evidence of intrapericardial adhesions in Case 6 was an interesting observation, but there was no apparent interference with the function of the heart The evidence of coronary damage shown by the electrocardiogram in Case 5 was the only late complication to appear

SUMMARY

1 Over a 2 year period 7 cases of injury to the heart and pericardium were treated in the Louisville City Hospital Five patients recovered and 2 died

2 Two patients recovered without operation In 1 pneumohemopericardium was observed

3 Five patients required major surgical treatment In 4 the heart was injured 3 had stab wounds of the left ventricle, 1 had a gunshot wound of the right ventricle In the other extrapericardial compression of the heart by an anterior mediastinal hematoma occurred

4 Two patients with symptoms due to prolonged cerebral anoxemia secondary to cardiac compression were treated, recovery occurred in 1, but death in the other

5 A transpleural approach utilizing modifications of Spangaro's incision was used in all but 1 patient. Because of suspected injury to the right internal mammary artery, primary exploration was made in the latter instance to the right of the sternum, later cutting across the sternum and rongeuring away a triangular portion of the lower segment to obtain exposure of the right ventricle

6 Following operations for wounds of the heart and pericardium, it is felt that no external drainage should be used, instead a wide communication should be left between the pericardium and the pleural cavity to provide internal drainage If any considerable amount of fluid accumulates in the pleural cavity, it may be removed by thoracentesis

7 Postoperative care of patients with injuries to the heart and pericardium is important, but differs little from that of patients following other major thoracic procedures

8 Complications in this group were few 2 patients developed mild bronchopneumonia, 1 case of pertussis occurred on the seventeenth postoperative day, and the same patient showed evidence of late coronary damage by electrocardiogram One patient showed roentgenological evidence of intrapericardial adhesions in the region of the apex

9 Death in 1 case was due to hemorrhage In this instance it is felt that an autotransfusion might have saved the patient.

The writer wishes to express his appreciation to Drs. C. E. Bird and R. A. Griswold for their aid in preparing this report.

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AN AMBULATORY METHOD OF TREATING FRACTURES OF THE SHAFT OF THE FEMUR[1]

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A METHOD of treating fractures of the femoral shaft calling for only the briefest of hospitalization is of interest to both patient and attendant surgeon Such a reduction procedure should also appeal to a tax burdened public compelled to furnish long hospitalization for indigent cases To meet the standard of the present economic trend, which demands maximum function with minimum expense, a method providing early ambulation has been developed

Although the introduction of skeletal traction met many of the difficulties of obtaining approximation, it did not lessen the period of recumbency It has been our experience that the effectiveness of skeletal traction in attaining reduction is always in direct relation to the efficiency of its countertraction, and furthermore, we have found that countertraction can be best obtained by skeletal means. A single clinical observation will convince one of the superiority of skeletal countertraction over the older gravity methods of countertraction, the degree analogous to the marked advance of skeletal traction over skin traction

A new method which provides for immediate reduction is herein presented—based on a combination of efficient skeletal traction with the reliable skeletal countertraction, and immobilization attained by plaster encasement of the thigh only, with the benefit of normal motion at both hip and knee joints This type of immobilization calls for little after-care and confers a comparatively painless convalescence However, the most outstanding advantage is immediate crutch ambulation with the briefest of hospital stay

Feasibility of upper femoral transfixion The current idea that proximity to vital structures contra-indicates transfixion of the upper femoral fragment has hindered progressive treatment, whereas, a study of anatomical cross sections proves the contrary to be true, in that the normal lateral angulation gives such a superficial placement to the femur in the trochanteric area that it literally invites transfixion (Fig 1)

Dual skeletal countertraction The safest and the easiest approach to the upper femoral fragment is from its lateral aspect, but since it is impractical to transfix completely the upper thigh as the pin would encroach on the perineum, a specialized form of skeletal attachment was devised to control dual transfixion of the femur, yet only partial transfixion of the thigh (Fig 2) A half-pin insertion, similar in principle to that which we reported for fractures of the radius and ulna,[2] supplies skeletal countertraction However, a single half-pin of this type has limitations and cannot of itself overcome every femoral deformity, but when two half-pins are inserted into the upper femur at an angle to each other, the superior fragment is directly and absolutely controllable, so that every displacement is mechanically replaced This angular insertion of the half-pins literally "toe-nails" the proximal fragment to the guiding clamp, which holds these two short pins

Technique of dual superior insertions The uppermost half-pin is inserted obliquely in a distal and medial direction, from a point about the center of the lateral aspect of the greater trochanter (Fig 2B) This first half-pin, the trochanteric half-pin, permanently attached but rotating freely in the guiding clamp, is drilled in with a rotary motion of the right hand, while the left hand holds the half-pin clamp parallel to the thigh The oblique hole in the lower end of the clamp provides the guiding agency for the insertion of the second short pin or the locking half-pin, which is inserted into the shaft at an angle to the trochanteric half-pin (Fig 2C) This half-pin may be inserted by hand, but usually the cortex is so dense that it is necessary to resort to a carpenter's drill. To provide for extra leverage a large hand drill with handles has been devised, to be used in ordinary bone drilling and for insertion of Steinmann pins or Kirschner wires Both half-pins *should completely transfix the femur* This fixed angular insertion of the dual half-pins is the crux of the successful mechanical control of the upper fragment

The half-pins, which are made in large, medium, and child sizes, are fashioned with shoulders to ensure against overinsertion, but no harm is incurred by projecting well beyond the medial border of the shaft, or even by passing through the epiphyseal lines The occasional difficulty in locating the borders of the greater trochanter in the obese subject may be overcome by needling with a Kirschner wire, or a spinal puncture needle Before the fixation or locking half-pin is inserted, it is advisable to locate the shaft of the upper frag-

[2]Anderson Roger Fractures of the radius and ulna. A new anatomical method of treatment. J Bone & Joint Surg , 1934, 16 379-393.

[1]Presented before the annual meeting of the American Academy of Orthopedic Surgeons, New York, January 13-16, 1935

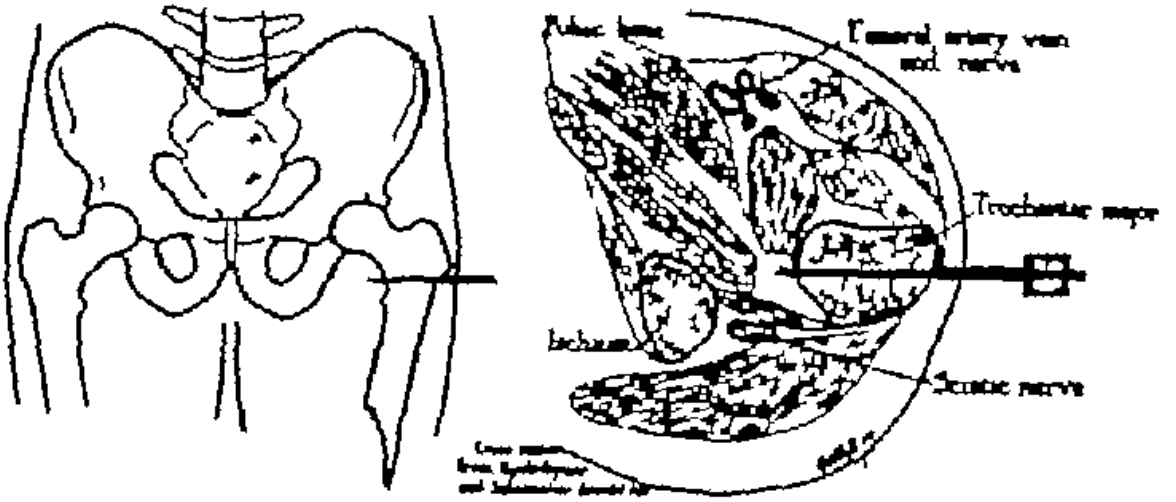


Fig. 1. Cross section through left femur at level of the distal border of the greater trochanter. Note superficial location of greater trochanter and wide *margin of safety between medial border of the* femur and the sciatic nerve and the femoral vessels

ment by probing with a Kirschner wire (Fig. 2A). The location and depth of insertion of the half-pins should be checked by fluoroscopic or film examination. Prior to roentgenography coverage of the half pin assembly with a sterile towel is advised so that, if necessary, the fixation half-pin can be drilled in deeper or both half-pins immediately withdrawn and reinserted. Sterile dressings around the pins are held by a few turns of unsterile sheet wadding.

Distal transfixions. A distal transfixion is made at the superior border of the condyles. However, to supply positive fixation with plaster encasement of the thigh alone, this distal insertion is supplemented with a second pin or wire through the shaft at a point about 2 inches above the first transfixion. It should not be placed parallel with, but at a slight angle to, the axis of the first distal transfixion. Here, again, especially in the supracondylar fractures, the borders of the distal fragment may be located by probing with a fine Kirschner wire from the lateral aspect. Hemorrhage from probe or pin wounds calls for no care, but one should keep in mind the sparse course of the femoral artery. The type of Steinmann pin used is only 4/32 inch in diameter and although special stainless steel renders it both flexible and strong, we are, nevertheless, making more use of Kirschner wire, since devising a simple means for tightening wire. Our wire tautner of stainless steel is so small and light that after incorporation in the plaster case it can be easily carried around covered by the split trousers.

This double pair of transfixions (Fig. 7C) not only supplies skeletal countertraction and traction, but provides means for separate and direct management of each fragment. The half pins through their angular insertion furnish a handle for universal manipulation—the same as a bone clamp. Traction for reduction can be supplied by either a fracture table or a specially designed splint for fractures of the femur.

Fracture table technique. After the patient is placed on the fracture table and his feet are bandaged to the traction stirrups, the thigh is surgically prepared for the transfixions—the superior half-pins being inserted first. Reduction by traction plus manual manipulation of the transfixions is roentgenographically checked before the application of a snug plaster case from the crest of the thum to the knee.

Anatomic splint technique. To facilitate reduction with accuracy and mechanical precision and to hold apposition independently of the uncertain human element while applying plaster, we devised an apparatus—a fracture robot (Fig. 4). This mechanical assistant—termed the anatomic femur splint—can be readily assembled by using the automatic leg splint as a chassis, in which instance the universal bracket with rotating arc and base plate is attached to the upper end of the leg splint.

The apparatus is so constructed that every mechanical manipulation, including rotation, is carried out in the normal anatomical manner. All adjustments of the superior fragment are made on an axis corresponding with the center of the head of the femur, while lower fragment displacements are mechanically managed with the center of the shaft as the axis (Fig. 4).

To provide better exposure for anteroposterior fluoroscopic examination, an adjustable aluminum leg stand has been designed which can be quickly attached to the upper end of the splint. In this event, the operating table or cart is utilized only

for the purpose of holding the head and shoulders, for the buttocks are supported by the sacral rest, the leg on the injured side held by the calf-support, while the splint *per se* holds the fractured thigh, the uninjured extremity being hammocked in the well thigh support, readily attached to the base

ROUTINE REDUCTION

Preparation of the patient For the complete management of the fracture, the patient need not be removed from the cart on which he was admitted After the initial roentgenogram, the hip on the injured side is brought well over the edge of the cart, while the assistant exerts manual traction on the injured leg, this slight traction is continued up to actual placement in the splint (Fig 5A) Meanwhile both upper and lower thigh receive surgical preparation preliminary to transfixion, as does the fracture site when a local anesthetic is used Incidentally, plaster bandages should be procured of a quality equal to the best slow setting commercial brands, when cold salt free water is preferred

The superior half-pin transfixions are first inserted and while their location and depth are being roentgenographically checked, the distal transfixions are placed

Placement in the splint In fastening the thigh to the splint, the patient is elevated a box 10 to 12 inches high is placed under the head and shoulders, and the buttocks are raised on the sacral rest, the calf on the injured side is held by the calf support, the non-injured extremity rests in the well thigh support (Fig 5B) To facilitate the attachment of the half-pin clamp, the universal bracket lock nut (Fig 4, *h*) and the pivot nut (Fig 4, *c*) are first loosened, so that the rotating arc can be swung and revolved into position as close as possible to the half-pin unit. Before the half-pin assembly can be fitted into the slot of the rotating arc, it may be necessary to lift or turn the half-pin clamp itself and to readjust the height of the sacral rest or to shift the buttocks laterally Either one of the distal transfixions is the means whereby attachment is made to the horseshoe at the knee end It is frequently advisable to wrap a plaster bandage around the distal insertions prior to reduction, in order to prevent the thigh slipping sidewise on this transfixion during the manipulative reduction

Traction is exerted with the swivel nuts loosened (Fig 4, *h*, *c*, and *m*), and these nuts are usually not tightened until reduction is completed To hasten reduction by either manual or mechanical manipulations, excessive traction is first employed, which tends to remove any interposed muscle

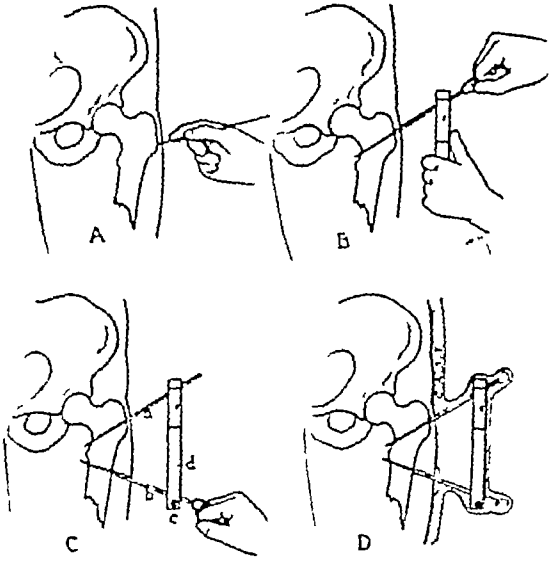


Fig 2 A, Borders of the greater trochanter outlined by needling with a Kirschner wire B, Oblique insertion of the trochanteric half pin C, Transfixing the shaft with the locking half pin Note angular insertion D, The half pin unit incorporated in the plaster The dual half-pin assembly is made in three sizes large, medium, and child

But in displaced spiral fractures, the fragments should be mechanically manipulated or unlocked so that the fractured surfaces face each other before traction is exerted In either instance, *all overtraction should be released* before the thigh is encased in plaster When reduction has been finally checked by film examination, the plaster is applied from the crest of the ilium down to a few inches below the knee Snug application of the cast —padded or unpadded—and firm incorporation of the pins, or wire tautnor to prevent all movement or loose play of thigh on pins, are tantamount to minimal after-care Plaster posterior to the knee joint and over the patella is at once cut out. Hence, this method permits movement at the knee joint as well as at the hip

Allowing a few minutes for setting of the plaster, the apparatus is removed from the patient by loosening all the lock, swivel, and thumb nuts preliminary to lifting the distal transfixion from the lower horseshoe, whereupon the cast is pulled medially, thus freeing the superior half-pin clamp from the rotating arc The pin ends are then covered with corks and plaster

After-care Circulation in the foot should be watched, though splitting and spreading of the cast is seldom necessary due to the fact that immediate reduction and immobilization reduces the

cause of further edema, besides minimizing shock. Recession of swelling calls for no attention as immobilization relies not at all upon the snugness of the cast around the fracture but entirely upon this specialized form of dual transfixion units.

Precaution to maintain end-to-end contact in adult cases Undue separation of the fragments from excessive extension delays union. Hence, the precaution maintain reposition with contact *even at expense of slight overlapping* Not infrequently subsequent absorption of the ends of the fragments results in separation which is revealed only by taking repeated roentgenograms. This likewise indicates decrease on traction, released by removing a thin transverse section of the cast between the transfixions.

Ambulation. *Crutch ambulation is allowed with* recovery from shock and drying of the cast. At first no body weight on the injured leg is allowed, but when confidence has returned, the patient is permitted to leave the hospital, fully dressed. At this time the inner seam of the trouser leg is split for better cast coverage. In a few weeks, or as soon as callus is revealed, a cane or single crutch may be sufficient, though in another week or so even that support may be discarded. However in the rare case, with the first roentgenographic evidence of bending of the pins with bowing at the fracture site, direct weight bearing should be postponed. After removal of the cast and transfixions, subsequent weight bearing protection with observation is routinely carried out.

The period of plaster immobilization—usually from 5 to 12 weeks—depends on that variable element, callus formation. Insertion wounds should receive no attention until removal of the pins or wire, which is accomplished by the uncovering and loosening of the fixation pin bolt, so that this half-pin can be withdrawn with a rotary movement. A circular cut through the plaster about 2 inches away from the half-pin assembly is then made to free it from the cast, whereupon this plaster island with its enmeshed trochanteric half-pin and half-pin clamp is easily pulled away in the direction of the axis of the trochanteric half-pin Both distal transfixions are removed in regulatory manner

A slight absorption around the half-pins, usually from failure to transfix the medial cortex completely may occasion pain in the region of the trochanters, but only in the exceptional case where there is severe pain is it necessary to withdraw and reinsert the half-pins to the proper depth. In some cases movement at the knee and hip joints will cause pain and a purulent discharge, which is due to pulling of the skin against the pins. Such a discharge appearing a few weeks after the pin insertion is not a cause for concern because it is usually just a sterile reaction from movement of the skin around the transfixions. Such discharge from irritation does not call for a change of dressings around the pins but it may be advisable to keep the patient quiet for a few days. Even in these cases the wounds heal in a few days after the transfixions have been removed.

SUBTROCHANTERIC FRACTURES

Although previously femoral shaft fractures in general have been troublesome, subtrochanteric fractures proved to be the most trying because of the difficulties in overcoming the triple displacement of the short upper fragment, abduction external rotation and flexion. But when direct control is obtained through the dual half-pins and with the strong mechanical manipulatory power of the splint, correction of this refractory displacement is a relatively facile performance. As this upper fragment is usually short, the trochanteric half-pin should be started into the superior lateral border of the trochanter or a smaller half-pin unit should be used. The marked medial displacement of the upper end of the distal fragment presents an additional problem in the unique spiral trochanteric fractures in which the lesser trochanter remains a part of the lower fragment. This can now be overcome by an oblique insertion of the second or so called upper distal transfixion, slightly closer to the anteroposterior than the lateral plane at a level about 4 to 5 inches above the knee. The axis of this wire or pin should be from the anterior medial surface of the thigh to the posterior lateral aspect. Traction on this oblique pin in a lateral direction overcomes the medial displacement, and correction is maintained by routinely embodying the transfixions in the cast.

SUPRACONDYLAR FRACTURES

These stubborn fractures no longer require treatment with the knee in flexion. With this new technique the upper pin or wire of the distal pair of transfixions is placed in the horseshoe then, with the hand over the knee joint, pressure is exerted downward until the posterior angulation is corrected. Otherwise, correction is mechanically obtained through an accessory device, a pair of side-arm extensions, which are attached to the distal horseshoe. Either mode of procedure is followed by routine reduction. The incorporation in plaster of both sets of dual transfixions prohibits a recurrence of the posterior femoral displacement.

Fig 3 Mr A S, fracture in the upper third was able to walk with crutches on the second day after operation

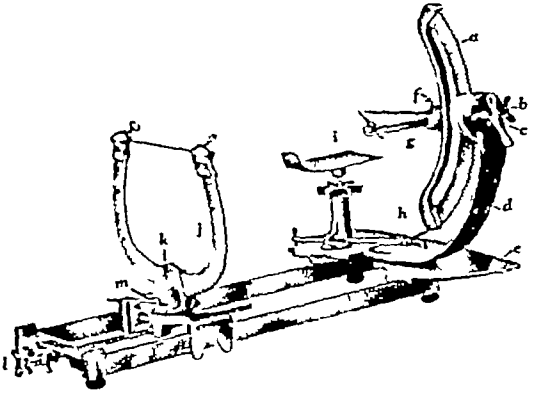
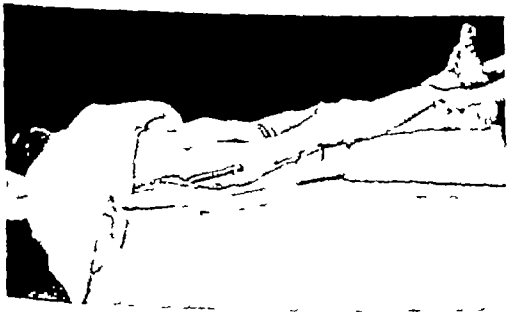
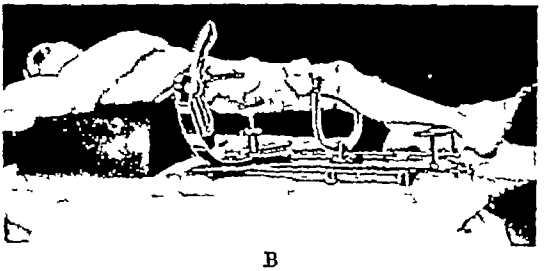


Fig 4 The anatomic femur splint whereby correct rotation through anatomical center at hip is mechanically accomplished by turning finger nut, *b*, abduction and adduction deformities are overcome by swinging the bracket *d* which is pivoted under center of hip joint and locked with nut at *h* correction of flexion or extension displacements at the hip are made upon the pivoting nut, *c* The distal horseshoe base, *k* is swiveled whereby sidewise displacements can be alined and anatomical rotation effected through rotating the teeth on its under side The rod, *l*, supplies traction The well thigh and calf supports are illustrated in Figure 5



A



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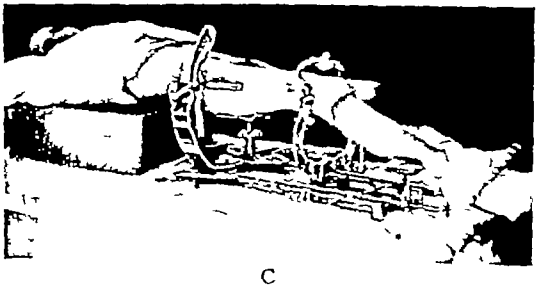

C

Fig 5 Illustrating steps in routine reduction A First, the trochanteric half pin is forced diagonally into greater trochanter after which the shaft of the femur is completely transfixed by the locking half pin and the clamping bar nut then tightened, second sterile dressing around the pin wounds are held in place with sheet wadding B A 12 inch box placed under the head and shoulder, the leg rested on the padded calf-support, the felt-covered sacral rest adjusted to the individual, the well thigh hammocked in the well thigh support is not clearly discernible in this illustration By tightening the thumb nut the dual half pin clamp is fastened into the rotating arc When either one of the distal transfixions has been connected to the splint, mechanical traction is instituted immediately, while the pivot nut (Fig 4, *c*) and the lock nuts (Fig 4, *h* and *m*) are left loose C, Reduction is perfected by traction power of the splint and mechanical manipulations, after roentgenographic check plaster bandage is applied from crest of ilium to knee, firmly incorporating the half-pin unit and the distal transfixions About 10 minutes later when plaster has set, the thigh is removed from the splint and the protruding ends of pins or tautnor are protected by corks and plaster Crutches are permitted when the plaster is dry

A B C

Fig 6 Mr K C 5 month fracture t junction of middle and lower third of right femur reduced elsewhere on two different occasions Referred to us with malunion, which on manipulation refractured with separation of the fragments A, Lateral view through cast revealing loss of apposition B, Posterior displacement corrected without open operation by pulling anteriorly on the wire Not pin distal to tuberosity C, Anteroposterior roentgenogram illustrating position of the femoral half pins Space between fragments due to presence of old callus

COMMINUTED FRACTURES

Comminuted fractures are as a rule routinely reduced but for that unusual type in which the adductor muscle pulls the large loose central fragment medially it becomes advisable to cut the cast out on the medial side when the swelling starts to recede A roll of sheet wadding placed over the medial aspect of this fragment is then strapped snugly in place with a bandage.

COMPOUND FRACTURES

When the anatomic splint is utilized both as a reduction and an immobilization agent, a compound fracture of the femur is amenable to any current method of treatment. The lesion can be thoroughly cleansed and closed with primary suture, or it can be packed with Orr's vaseline gauze. On the other hand open air treatment, chemical lavage, or Baer's maggot method are all feasible, since the thigh may be left fully or partially exposed in the splint as long as required Placement of the patient in bed after the splint has been applied is detailed in a previously published paper [1]

[1] Anderson, Roger Femoral bone long, thinning Am J Surg 1948, 77 479

MAL UNION AND NON-UNION

The splint is a valuable adjuvant to the treatment of mal-union or non-union, because the apparatus, assembled or separated into its major parts, may be wrapped in a sheet and sterilized in the autoclave in which event all mechanisms are regulated in a sterile manner An equally adequate but more rapid technique is to proceed by utilizing an unsterilized splint, transfixing the femur and placing the thigh in the apparatus as described herein. Any necessary operative manipulation is accomplished by a lateral approach to the femur through a slot in a sterile sheet adjustments on the apparatus itself are made from behind the sheet by a non-sterile assistant.

FRACTURES OF THE SHAFT OF BOTH FEMURS

This seemingly complex problem is simply solved, because one shaft at a time is reduced by routine technique. With two such major fractures only a brief hospitalization is obligatory since there can be no danger of loss of apposition with each fragment nailed to the cast. If desired, as in the case of an associated fracture of the pelvis,

A B C

Fig 7 Mr C J A, Lateral roentgenogram before reduction, B, after reduction (In our earlier cases the upper half-pin was transversely inserted at the distal border of the greater trochanter) C, Patient was up and about a week after reduction Plaster is cut out in back of knee to permit flexion

the plaster may be extended upward to form a double spica Revolutionary as it may seem, even in this day of modern fracture treatment, these patients may be accorded the immediate privilege of the wheel chair and a comparatively early use of crutches with the assurance of a relatively painless convalescence

FRACTURES OF THE FEMORAL SHAFT AND OF THE SPINE

In the event of a double fracture, such as that of the shaft in association with a fracture of the spine, a single spica cast provides sufficient immobilization for both fractures to permit early ambulation

FRACTURES OF FEMUR AND TIBIA

A fracture of the femoral shaft in association with fractures of both bones of the same leg can be reduced by slightly varying the technique The fractured femur is reduced first, during which period the lower leg should be steadied A single distal femoral transfixion, inserted obliquely, supplies the agency for traction and fixation The plaster segment incorporating this pin or wire is applied with the knee in extension, from the femoral fracture site to the level of the tibial fracture When the fracture of the femur is reduced, the cast is extended up to the crest of the ilium In order to reduce the tibial fracture by our double pin method,[1] the splint is removed from the thigh just as soon as the plaster sets, and the apparatus is converted into an anatomic leg splint by substituting our standard horseshoe for the universal bracket and base plate The means of skeletal traction for the tibial reduction has already been supplied at the time the femur was transfixed, when an extra pin or wire was inserted through the tibia above the ankle The distal femoral pin may be used for the tibial countertraction agent, but if desired, another transfixion through the upper tibia may be made for countertraction The lower leg is placed in the splint and after the mechanically obtained reduction is roentgenographically checked, the cast is extended down to the toes, to incorporate the tibial transfixion A walking stirrup is later adjoined with plaster Even with these multiple fractures early crutch ambulation is practical, since both upper and lower fractures are immobi-

[1] Anderson Roger An automatic method for treatment of fractures of the tibia and fibula. Surg Gynec. & Obst., 1934 58 639

A B C

Fig 8. A, Mr H B struck by a tree, received a spiral fracture of the shaft of the left femur crushing fracture of the first lumbar plus serious internal injuries with grave hemorrhage Continuous oozing necessitated week of intravenous feedings with transfusions On the twenty-second day he was up and walking in spica cast that immobilized both spine and femur Plaster extended to the mid-calf as only one pin was inserted through the distal fragment B Lateral view before reduction C, After reduction.

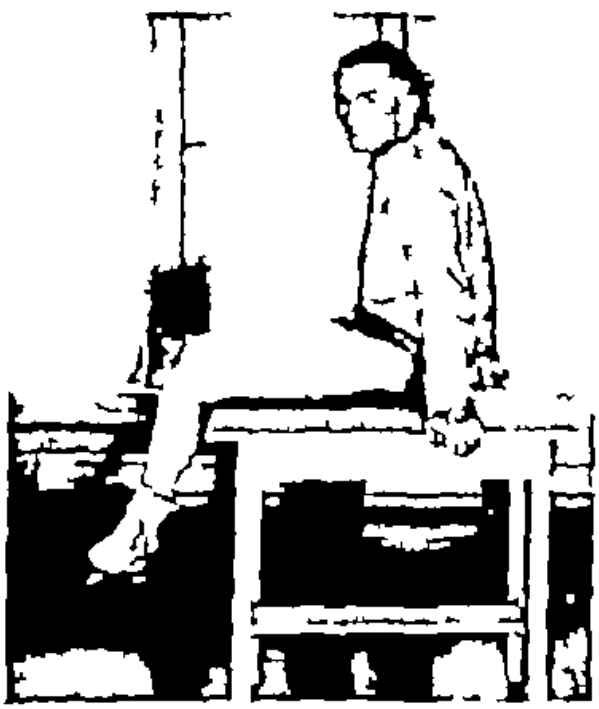

Fig 9 Mr H B The short cast demonstrates the advantages of active and passive motion at both knee and hip joints

fixed in the same cast, which extends only from hip to toes.

OPTIONAL TECHNIQUES

A single distal transfixion is a variation of the technique described, and such transfixion can be employed provided the cast is elongated to mid-leg—the cast preferably being made in two sections This plaster extension commensurates for the lack of the second distal insertion The lower or first plaster segment, which incorporates the single distal pin or wire extends from just below the fracture line to mid-calf During application of this plaster the knee is usually forced into and held in extension, a position better retained if the distal transfixion is put in obliquely to the transverse axis of the knee joint On completion of the reduction the plaster is extended up to the crest of the ilium thus incorporating the dual half pins

Dual half-pin transfixion of the distal fragment is also practical and these half-pins may be inserted from either the medial or the lateral side of the distal thigh.

A single superior transfixion with a single distal insertion can also be employed when the pin is

inserted according to our earlier technique for femoral bone lengthening, in which case a single pin or wire completely transfixes the upper thigh in an oblique anteroposterior direction In this technique, a spica from ribs to mid-calf is essential

Traction for the above modifications as for routine reduction may be furnished by either the fracture table or the splint,—preferably the anatomic femur splint Obviously, the table procedure has inherent difficulties the number of assistants required, the necessity of a fracture table with its fluoroscopic obstacles, to which is added the unreliable human element. The fundamental principles of reduction are identical for both table and splint, but with the table it is difficult to execute the manipulations of each fragment on the true anatomical axis

It is apparent that many variations and combinations of technique for either reduction or immobilization are feasible while operating on the same basic principles For example, half-pin insertions may be substituted for the usual distal transfixions While for reconstruction or congenital hip operations and for certain orthopedic conditions of the lumbar spine or pelvis the half-pin units may be used routinely, in bifurcation operation and for some fresh or ununited fractures of the hip the half-pins may be inserted into the upper femur below the trochanters We have also been treating fractures of the shaft of the humerus in accordance with the principles of dual half-pin control

WARNINGS

Our objective—a perfect roentgenographic reduction—can usually be obtained, and early restoration of function achieved, if the following factors are closely observed

1 Both fragments should be located by probing with a Kirschner wire

2 Half-pins should completely penetrate the medial cortex

3 Separation by overtraction should be avoided

4 Only the best plaster bandages should be employed

5 Repeated roentgenographic check

6 Insistence on early and strenuous daily exercise, plus active movements at both knee and hip

7 Painful convalescence is usually due to faulty technique and calls for correction

8 The axiom of the Fracture Committee, "It is the doctor behind the splint that counts in the treatment of fractures" should be kept in mind

SUMMARY

This new method of reducing femoral shaft fractures, based upon a specialized form of transfixion, requires plaster encasement of the thigh alone for immobilization A further advantage is the preservation of muscle and joint movement, which is brought about by non-immobilization of hip and knee joints plus early weight bearing Of paramount importance is the fact that crutch ambulation is immediately possible, thus reducing the patient's stay in the hospital Other important factors are the slight after-care required and the fact that the patient suffers little pain during convalescence Hence, we are brought closer to our ideal in the treatment of fractures the securing of maximum function with minimum expense and pain

TWENTY YEAR CURES OF CARCINOMA OF THE COLON

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PAUL F OLSON M D ROCHESTER, MINNESOTA
Fellow in Surgery The Mayo Foundation

We are not so constantly and impressively reminded of those individuals in whom carcinoma has been apparently eradicated as we are of those who have succumbed because of it.

The death rate attributable to carcinoma each year serves to augment the skepticism of both physicians and laymen regarding its curability To use the term cured" in connection with malignancy may seem at least hazardous, but those individuals who are alive for many years following removal of a malignant growth, without symptoms of recurrence would seem to have been more than temporarily relieved of their ailment

Doubt may reasonably exist regarding the ultimate outcome of some of the patients classed as having obtained 3 and even 5 year cancer cures, but those patients who are alive from 10 to 15 or 20 years after removal of a carcinoma of the colon may be classified, it seems, as permanently relieved of their original malignant lesion.

Cheever in a review of surgery of the colon made in 1930 at the Peter Bent Brigham Hospital, noted 1 patient who had survived for 10 years after a resection of the colon for carcinoma and 2 who had survived 12 years Another patient died 10½ years after operation and had no recurrence. Cheever also reported a patient who died of recurrence 10 years after the operation. Oughterson and Shelton in a review of the end-results of the treatment of carcinoma of the colon noted 2 patients who were still living 12 years after the resection of the colon Coffey in studying carcinoma of the rectum, called attention to 2 patients who had died without recurrence 17 and 13 years respectively after operation, and to 3 patients who were living 17 years, 11 years, and 10 years, respectively after resection Brown reported 1 patient living 10 years after operation.

It might add to the peace of mind of those who may be afflicted with malignant disease in the future if more emphasis were laid on the curability of carcinoma and if more specific instances were cited as definite proof of the contention With this in mind, we are reporting in some detail the operative and pathological records of a dozen patients who lived for more than 20 years after the eradication of carcinoma of the large intestine.

Inasmuch as carcinoma occurs with greatest frequency in the later decades of life many patients conclude their natural span of existence before 10 postoperative years have had time to elapse therefore the number of 10 year survivals are greatly reduced by causes other than carcinoma In making this report we wish to cite only instances of indisputable cures of carcinoma and therefore have included only patients who are living or who have lived without evidence of recurrence for more than 20 years after removal of carcinoma situated in the colon Twenty years of life without further trouble conceivably might not be regarded as a cure of cancer by the most exacting observer, but we feel sure that such an eventuality would be held in high regard by the patient

When one refers to a possible cure of cancer the question is immediately raised as to whether the original lesion really was cancer The question is a proper one. In the cases we are reporting the tissue was diagnosed as carcinoma by the pathologist at the time of operation The gross specimens have been preserved in the museum of surgical pathology They have now been re-examined, new microscopic slides have been made, and the diagnoses have been confirmed. Illustrations of some photomicrographs are included. A quarter of a century in formalin has interfered somewhat with the microscopic appearance of the tissue but it also adds to its interest.

REPORT OF CASES

CASE A man, aged 48 years, was operated on, April 30, 900 because of a carcinoma which involved the cecum and ascending colon Ten inches of the terminal portion of the ileum, the cecum, the ascending colon, and half of the transverse colon were removed The ends of the ileum and colon were closed and a side to side anastomosis was made T enty-one years and 7 months later, the patient reported that, "I have had and am now enjoying very good health for a man of my age. The gross specimen contained a carcinoma which measured 7 by 4 centimeters Microscopic study revealed an adenocarcinoma, grade 1 (Fig) No involvement of the lymph nodes was found

CASE A woman aged 49 years, was subjected to operation on March 7 1908, because of carcinoma of the cecum The cecum, the ascending, and half of the transverse colon were resected and side-to-side ileocolostomy was performed Twenty years and 1 month later the patient died The cause of death was not stated by her son, who was our

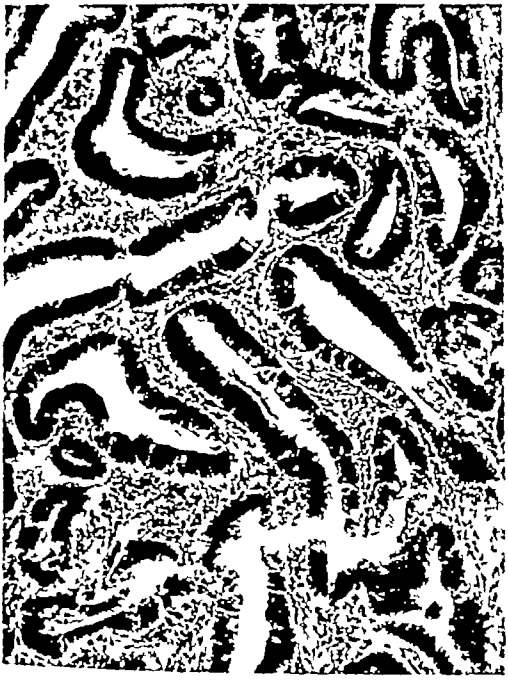

Fig 1 Photomicrograph of adenocarcinoma, grade 1, of cecum and ascending colon. ×100

Fig 2 Photomicrograph of adenocarcinoma, grade 1, of the cecum and ascending colon ×65

informant. Grossly, the adenocarcinoma measured 8 by 4 centimeters and microscopically it was grade 1 No involvement of the lymph nodes could be found

CASE 3 A woman, aged 49 years, was operated on, August 21, 1911, because of carcinoma of the cecum A loop of ileum was adherent to the growth Local mesenteric lymph nodes were involved by metastasis. Eight inches of ileum, in which there was a secondary growth, the cecum, the ascending colon, and 4 inches of the transverse colon were resected, and a lateral ileocolostomy was performed Twenty years and 3 months later, the patient was living and said that she was enjoying fine health for her age The carcinoma measured 5 by 7 centimeters, and microscopically it was grade 1 (Fig 2)

CASE 4 A man, aged 38 years, came to the clinic on October 15 1910, complaining of symptoms which led to the diagnosis of a tumor of the descending colon Exploration revealed a carcinoma of the descending colon Ten inches of the colon which contained the growth, was resected A loop of small intestine was adherent to the growth This also was resected Twenty years and 8 months later, the patient died following amputation of an arm, elsewhere The gross specimen of the colon revealed a carcinoma, which measured 5 by 4 centimeters Microscopically, the malignancy was grade 2 No metastasis to the local lymph nodes could be found

CASE 5 A woman, aged 64 years, was operated on, August 14, 1911, because of a tumor of the sigmoid flexure Twelve inches of the intestine was resected, and the ends of the colon and ileum were closed Lateral anastomosis was made The patient is well and active at 85 years of age Grossly, the carcinoma measured 4 by 3 centimeters, and microscopically it was grade 2 (Fig 3)

Fig 3 Photomicrograph of carcinoma, grade 2, of sigmoid flexure ×100

Fig. 4. Photomicrograph of adenocarcinoma, grade 2 of cecum and ascending colon. × 60

Fig. 5. Photomicrograph of carcinoma, grade 1 of sigmoid flexure. ×55

Fig. 6. Photomicrograph of adenocarcinoma, grade 1 of sigmoid flexure. × 60

Case 6. A man, aged 30 years, was subjected to exploratory laparotomy on September 30, 1907 because of tumor in the lower part of the sigmoid flexure. The growth had penetrated the bladder. The sigmoid flexure and portion of the bladder were resected. The gross specimen of the carcinoma of the sigmoid flexure measured 4 by 3 centimeters. No involvement of the lymph nodes was found. The patient was living at the time of inquiry 24 years and 1 month later. Microscopically the adenocarcinoma was grade 2.

Case 7. A man, aged 40 years, was operated on, March 6, 1910, because of a mass in the right lower quadrant of the abdomen. Exploration revealed carcinoma of the cecum. The cecum and ascending colon were resected. A lateral anastomosis was made between the ileum and transverse colon. The gross specimen contained a carcinoma which measured 6 by 4 centimeters. No metastasis to local lymph nodes could be found. Microscopic study revealed an adenocarcinoma, grade [illegible] (Fig. 4). The patient was living years and 7 months later.

Case 8. A man aged 54 years, was operated on, August 3, 1910, for an obstructing carcinoma of the ascending colon. Eight inches of the ileum, the cecum, the ascending colon, and half of the transverse colon were resected, and a lateral anastomosis was performed. Twenty-one years and [illegible] months later, the patient described himself as "still living but rather feeble." Grossly the carcinoma measured [illegible] by 3 centimeters, and microscopically it was grade [illegible]. No involvement of the lymph nodes could be found.

Case 9. A man, aged 4[illegible] years, was operated on, September [illegible], 1907 because of a tumor of the sigmoid flexure. Eight inches of the colon was resected. This revealed a carcinoma which measured 6 by [illegible] centimeters. Twenty-four

years later, the patient was in good health Microscopically, the malignancy was grade 1 (Fig 5)

CASE 10 A man, aged 53 years, was operated on, December 26, 1910, because of a tumor of the splenic flexure of the colon The splenic flexure and a portion of the descending colon were removed, and a lateral anastomosis was performed between the transverse colon and the sigmoid flexure. Twenty-one years later, the patient reported that he was living and in good health Grossly, the lesion measured 5 by 4 centimeters, and microscopically it was an adenocarcinoma, grade 1 No local metastasis was demonstrable

CASE 11 A woman, aged 56 years, was subjected to exploratory laparotomy because of a tumor of the middle portion of the sigmoid flexure Ten inches of sigmoid flexure was removed and an end-to-end anastomosis was made by the tube method Local lymph nodes were involved The gross specimen measured 7 by 2 centimeters The adenocarcinoma was grade 1, microscopically (Fig 6) The patient was alive and in "fairly good health" 20 years and 11 months later

CASE 12 A man, aged 49 years, was operated on, January 2, 1909, because of a mass in the ascending colon Eight inches of ileum, the cecum, and the greater part of the ascending colon were resected Grossly, the specimen revealed a carcinoma which measured 5 by 4 centimeters No metastasis to local lymph nodes could be demonstrated Microscopically, the tumor was an adenocarcinoma, grade 2 Twenty two years and 10 months later, the patient reported that he was living but "suffering from heart trouble"

In the 12 cases of carcinoma of the colon in which 20 year surgical cures were obtained, it is of interest to note that 10 patients were still living at the time inquiry was made The time elapsed since operation ranged from 20 years and 1 month to 24 years and 1 month

Two of the patients were operated on when they were in their third decade, 6, in their fourth decade, 3, in their fifth decade, and 1, at the age of 64 years Eight of the patients were men and 4 were women

In view of our experience with the microscopic grading of malignancy, we feel that it is a very significant observation that in all of these cases, the grade of malignancy was low In 6 cases the malignancy was grade 1, and in 6 cases it was grade 2 In no case in which the patient survived for 20 years was the malignancy found to be grade 3 or grade 4 In a recent review of 453 specimens of carcinoma of the colon at the clinic, we observed that in 14 per cent the malignancy was grade 1, in 61 per cent it was grade 2, in 18 per cent it was grade 3, and in 7 per cent it was grade 4 The malignancy was grade 1 in 50 per cent of the cases in which 20 year cures were obtained

A study was made of 453 pathological specimens to determine if possible the factors which influenced prognosis Data as to the length of postoperative survival were obtained for that number of cases and microscopic sections were made of the corresponding tumors Cases in which the patients did not respond to our letters of inquiry could not be included Consequently, the significance of the percentage of cures rests on the relative effect rather than on the absolute percentage of the grading From a study of 453 cases of carcinoma of the colon, it was found that 66 per cent of the patients who had carcinoma, grade 1, 54 per cent of those who had carcinoma, grade 2, 38 per cent of those who had carcinoma, grade 3, and 30 per cent of those who had carcinoma, grade 4, survived for 5 years These figures indicate the noticeable high incidence of 5 year survivals in the cases in which the grade of malignancy was low We feel that it is a very significant observation that of the patients who obtained 20 year cures all had a growth which revealed a malignancy of grade 1 or grade 2

Of the 12 cases in which 20 year cures were obtained, only 3 revealed metastasis to the local lymph nodes This observation is in accord with our studies of the entire 453 cases, in which it was observed that in the cases in which there was no demonstrable extension to the local lymph nodes, the patients as a group, had almost twice as good an outlook as did those in whom there was metastasis to the lymph nodes Only 33 per cent of patients who had involvement of the regional lymph nodes lived for 5 years This is in sharp contrast to the 60 per cent of 5 year survivals among those who did not have any involvement of the regional lymph nodes

Having observed that both the grade of malignancy of the primary lesion and the presence or absence of metastasis to the local lymph nodes had an influence on the prognosis of carcinoma of the colon, it became a problem of considerable interest to ascertain whether or not the one factor influenced the other The incidence of involvement of the lymph nodes, therefore, was computed separately for the groups of cases falling into each of the four grades of malignancy The 453 cases were studied from this approach and metastasis to the local lymph nodes was found to occur almost twice as frequently from primary lesions that were of grade 4 malignancy than from those which revealed a malignancy of grade 1 The incidence of metastasis to the regional lymph nodes was 28 per cent in cases in which the carcinoma was grade 1, 30 per cent in cases in which the carcinoma was grade 2, 36 per cent in cases in which the carcinoma was grade 3, and 53 per cent in cases in which the carcinoma was grade 4

From the pathological study of the 12 cases in which 20 year cures were obtained, as well as

from the whole series of 453 specimens of carcinoma of the colon It is evident that the grade of the primary malignancy and the presence or absence of metastasis to the local lymph nodes influence the ultimate postoperative prognosis to an appreciable extent.

SUMMARY

The surgical removal of carcinoma of the colon holds out a very definite prospect of complete cure. To establish the accuracy of this contention, 12 cases are reviewed in detail, with surgical and pathological observations. In all of these cases the patients survived the operation for more than 20 years, and 10 patients were still living at the time of the last inquiry It is of interest to note that in 2 of these cases, loops of small intestine had to be resected on account of direct extension of the primary growth. In 1 case, the bladder had been encroached on by a carcinoma of the sigmoid flexure and had to be resected partially

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OBSTRUCTIVE CHOLECYSTITIS

With Particular Reference to Acute Obstructive Cholecystitis and Its Sequelæ[1]

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SUDDEN complete obstruction of the cystic duct, usually produced by impaction of a calculus, results in retention of bile in the gall bladder If the obstruction is maintained and if the gall-bladder walls are not seriously infected, the contents of the vesicle are absorbed by the lymphatics and venous channels After a few weeks, only clear colored, mucoid material (white bile) and stones remain This condition is called hydrops

But if the obstruction is not released early and if the gall-bladder walls are actively infected, the acute pathological process progresses A few days, or even hours after the obstruction occurs, bile flaked with pus may be found in the gall-bladder cavity and the walls become infected, edematous, and covered with fibrin, or may be studded with minute abscesses Lymphatic and venous circulation is disturbed and patches of localized gangrene frequently terminating in perforation, may ensue During the development of these changes, the pathological process has progressed so rapidly that bile is still encountered in the gall bladder It is rather surprising that we have no term descriptive of this condition The term "obstructive cholecystitis" refers to the complete obstruction of the cystic duct, but does not indicate whether the gall bladder is filled with bile, mucus, or pus, nor does it describe any inflammatory condition of the gall-bladder walls I suggest that the term "acute obstructive cholecystitis" be applied to the suddenly obstructed and acutely inflamed gall bladder which is still filled with bile The adjectives fibrinous, phlegmonous, and gangrenous may be added to define the pathological condition further, if desired Thus we may have acute fibrinous obstructive cholecystitis, acute phlegmonous obstructive cholecystitis, etc The terms "hydrops" and "empyema" are used to designate the obstructed gall bladders, filled with mucus or pus Acute and subacute exacerbations of these are indicated by these adjectives Thus we have acute hydrops, subacute empyema, etc

The initial lesion in all forms of obstructive cholecystitis is, in my opinion, an acute obstructive cholecystitis Hydrops and empyema are the results of prolonged obstruction and develop from an acute obstructive cholecystitis I have seen the development of a hydrops in an operatively removed specimen of subsiding acute obstructive cholecystitis when the gall-bladder contents were half bile and white bile One frequently sees the development of an empyema from an acute obstructive cholecystitis when the contents of the gall bladder are pus mixed with a small amount of bile And more frequently, one encounters an empyema developing from an infected hydrops as shown by an admixture of pus and white bile in the gall bladder Obviously, these three lesions, acute obstructive cholecystitis, hydrops, and empyema are stages in the development of a pathological process which has obstruction as its common antecedent. The presence of infection at the time of the initial obstruction, or its introduction after the obstruction has become chronic determines what type of obstructive cholecystitis will occur, or may be found at operation

Therefore it is evident that the progression of the pathological condition is dependent upon the time element and upon the presence of old or recent infection If these could be determined clinically, the type of obstructive disease might be anticipated It is usually impossible, however, to determine which colic, if any, resulted in complete obstruction and it is even more difficult to decide when the onset of fresh infection has occurred Under these circumstances, it is not surprising that so few correct pre-operative diagnoses of the exact stage of the process are made (Table I) In the chronically obstructed lesions the gall bladder is usually palpable and the incidence of correct diagnoses is high, the X-ray accounted for a number of these But when an acute flare-up occurred in the chronically obstructed gall bladder, the ability of the physician to decide whether the lesion was an acute hydrops or an acute empyema was greatly decreased In the series here reported, the error was nearly 50 per cent And in the new, acute obstructions (i e, acute obstructive cholecystitis), it was still more difficult to estimate whether the gall bladder contained bile, mucus, or pus When we attempted to anticipate the complications of obstructive cholecystitis (gangrene and perforation), our errors were very great, especially in the acute obstructive cholecystitis cases

The majority of our patients suffering from obstructive cholecystic diseases appeared at the hospital when an acute exacerbation of the

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TABLE I.—PRE-OPERATIVE DIAGNOSIS

Pathology	Total No. of cases	Pre-operative diagnosis	Corrected diagnosis, at operation
Obstructive cholecystitis	[illegible]	correct	
Hydrops, acute or chronic	54	6 correct	
Empyema, acute or chronic	17	4 correct	
Perforated obstruction	3	"acute cholecystitis"	
Perforated hydrops	3	correct	
Perforated empyema	6	correct	
		"empyema"	
		"appendicitis"	
		"pelvic abscess"	
	21	Acute cholecystitis	Obstructive cholecystitis, hydrops or empyema
	16	Incorrect or "implied"	Obstructive cholecystitis, hydrops or empyema
	4	Empyema	empyema with perforation
			acute hydrops
			acute exacerbation of chronic cholecystitis
		Chronic cholecystitis	chronic empyema
			acute hydrops
		Hydrops	Chronic cholecystitis with stones
	1	Perforation	obstructive cholecystitis
			empyema
			hydrops
			acute exacerbation of chronic cholecystitis with stones

chronic lesion developed. Local tenderness and abdominal rigidity were present in most of the cases and a diagnosis of acute cholecystitis was usually made. This was unfortunate, for as soon as the diagnosis of acute cholecystitis was accepted most of the staff treated the patient conservatively "to await subsidence of the acute infection. In a previous paper (5) I showed that the mortality of excessive conservatism was great (56 per cent) The present study shows that earlier surgery can greatly reduce that figure, for we now have a mortality of 15 per cent in obstructive cholecystitis. Particularly encouraging are the series of perforations in these gall bladders. Formerly 8 gall bladders perforated while under observation in this series only 2 ruptured in this manner Our mortality from perforated gall bladders has dropped from 48 per cent in 1932 to 26 per cent at present This is due mainly to earlier operative intervention With delayed operation, the mortality in perforated gall bladders was 55 per cent in 1932 and with early operation 41 per cent At present, it is 44 and 11 per cent, respectively These figures are instructive, for our operative staff has not changed materially during this interval.

From this evidence, it would seem that our mortality might be further decreased if we could operate upon obstructive cholecystitis earlier Inasmuch as 95 per cent of all perforations and gangrenes occur in the obstructed gall bladder it is necessary that we distinguish the obstructed from the non-obstructed forms of acute cholecystitis. This should be possible, but it is difficult as evidenced by preceding data and by Table I.

The first step in improving our diagnostic perception is to clarify the nomenclature. The term, "acute cholecystitis," implies an acute obstruction, or an acute inflammation in the gall bladder The obstructive types of acute cholecystitis are the most serious and therefore should be distinguished, clinically, from the non-obstructive forms And, if possible, the obstructed lesions should be differentiated in their three forms, namely those containing bile, mucus, or pus. We would then have the acute obstructions and the acute exacerbations of chronic obstructions named as acute obstructive cholecystitis and acute hydrops or acute empyema, respectively The terms subacute and chronic hydrops or empyema, depending upon their content, may be used to designate the less acutely inflamed gall bladders. All

TABLE II—OPERATIONS AND MORTALITY

Pathology	Cholecystectomy	Cholecystostomy	Total	Mortality
Acute fibrinous obstructive cholecystitis		2	2	0
Acute phlegmonous obstructive cholecystitis			0	0
Acute gangrenous obstructive cholecystitis	1		1	0
Acute obstructive cholecystitis with perforation	1	2	3	0
Subacute obstructive cholecystitis	1		1	0
Acute hydrops	12	1	13	3
Acute hydrops with perforation	1	2	3	0
Subacute hydrops	-	1	3	0
Chronic hydrops	5	0	5	0
Acute empyema	3	3	6	0
Subacute empyema	1	1	2	1
Chronic empyema	1	2	3	1
Acute or subacute empyema with perforation	3	3	6	3
	33	18	51	8 (15%)

other acute cholecystic lesions, i e, the non-obstructed, could then be called acute cholecystitis with defining adjectives, as catarrhal, gangrenous, phlegmonous, acute exacerbation of chronic cholecystitis, etc In this way we will have called attention to the serious forms of acute cholecystitis by defining them as obstructive or not These terms, with one exception, have been available in the past, but they have not been fully utilized with this understanding In the series here discussed on our service at the San Francisco Hospital, 10 cases of acute obstructive cholecystitis were encountered, none of which was correctly diagnosed before operation Twenty-four cases of hydrops were met with, only 27 per cent were accurately diagnosed and only 7 per cent of 17 cases of empyema When efforts were made to diagnose the complications of obstructive cholecystitis, perforation was cited in only 3 of 14 instances That we are attempting to anticipate perforation, however, is noticeable, for in 5 instances a diagnosis of rupture was made when it was not found at operation (Table I) Is our diagnostic acumen dulled, or is it really impossible to make a detailed pathological diagnosis before operation? For the past several years we have made every possible effort to anticipate correctly the type of acute cholecystitis which may be encountered at operation As many of the staff as possible see the patient and commit themselves before operation Only too often we diagnose empyema when the case is one of hydrops and *vice versa* The acutely obstructed gall bladder, filled with bile, has given us even greater difficulty Should we, then, attempt to differentiate the three types of obstructive cholecystitis, or shall we be content with distinguishing the obstructed from the non-obstructed types of acute cholecystitis? I believe we should strive to accomplish the former but it is necessary to do the latter

The history of the biliary distress, the presence of a tender mass, the height of the fever curve, and the degree and character of the leucocytosis when carefully evaluated will usually make possible a differentiation between obstructed and non-obstructed lesions in acute cholecystitis In chronic obstructive cholecystitis, i e, hydrops and empyema, the history of intermittent trouble and the presence of a globular, movable mass at the right costal margin usually suffice for a correct diagnosis But the task of distinguishing the acute obstructions from the acute exacerbations of chronic obstructions may be most difficult The data that follow will assist us, in some measure But if the acute cholecystitis is so marked that abdominal rigidity prevents the palpation of a mass and therefore prevents us from differentiating the obstructed from the non-obstructed forms of acute cholecystitis, as well as inhibiting the differential diagnoses of the 3 types of obstructive cholecystitis, then, I believe we should observe the patient for 6 to 48 hours before instituting surgical therapy If fever, leucocytosis, tenderness, and rigidity have not definitely subsided in this period, surgical exploration should be done, for we know we are dealing with an advanced, acutely inflamed gall bladder Under this policy our mortality has decreased

The present review embodies 149 consecutive gall-bladder operations performed on the Uni-

TABLE III.—AGE AND SEX

	Acute obstructive cholecystitis		Hydrops		Empyema	
	No.	%	No.	%	No.	%
Male	3	30	4	17	4	33
Female	7	70	19	83	11	67
Ages						
20–30			6	25	1	8
30–40		20	3	13	3	25
40–50	3	30	4	17	5	42
50–60		20	4	17	3	25
60–70	3	30		4		
70–80		20	2	8		8

TABLE IV.—DURATION OF CHRONIC SYMPTOMS

	Acute obstructive cholecystitis		Hydrops		Empyema	
	No.	%	No.	%	No.	%
None	3	30		8	2	17
1 mon.		20	4	17	1	8
2 yr.	2	20		4		4
3 yrs.		20				
4 yrs.		20		8	2	20
5 yrs.	2	20		8		17
10 yrs.			2	13		4
15 yrs.			8	33	5	50

TABLE V.—DURATION OF ACUTE SYMPTOMS

	Acute obstructive cholecystitis		Hydrops		Empyema	
	No.	%	No.	%	No.	%
None						
1 day		20	2	20	1	8
2 days		20	4	17	4	30
3 days		20		8	1	8
4 days		20	1	8		8
5 days						17
6 days						8
7 days		20		17		
1 wks.		20		8	3	25
2 wks.				8		17
4 wks.						17
6 wks.						
8 wks.						

vernity of California service at the San Francisco Hospital during the past 6 years, 51 of these were for obstructive cholecystitis. This is an unusually high percentage of acute cholecystitis cases. It is accounted for by the fact that it is a county hospital, that the Emergency Hospital Service for San Francisco brings the acute cases to this Hospital and by the fact that less than one-fourth of the total patients having cholecystic disease were subjected to surgery

Most of the obstructive lesions were encountered in women (72 per cent) and the major number of patients were in the age group of 40 to 60 years (Table III) Eight per cent of the patients having hydrops 12 per cent of those with empyema and 30 per cent of those having acute obstructive cholecystitis stated that they had never suffered from any symptoms that might be even suggestive of previous cholecystic disease The great majority however of those having hydrops or empyema gave a history characteristic of gallbladder disease for many years In contrast, those patients having acute obstructive cholecystitis had short periods of biliary distress (Table IV) This clinical data confirms what might be expected from the pathology for hydrops and empyema are chronic lesions while acute obstructive cholecystitis is a recent and relatively sudden catastrophe. Of course, in some instances the patients had had gall stones for many years before one suddenly became impacted in the cystic duct.

The duration of acute symptoms follows the normal expectancy when viewed in the light of the pathology Most of the hydrops and empyema cases had their present illness for several days or even weeks before they entered the Hospital. Most of the patients having acute obstructive cholecystitis had their acute symptoms for 4 days or less (Table V) These same relations were evident in the history of qualitative food distress, belching and flatulence. But a large percentage of patients with acute obstructive cholecystitis and an unexpected percentage of those with hydrops denied ever having had any of these symptoms during either the acute or chronic stages of their diseases (Table VI).

The temperature curves were highest in the empyema cases and lowest in the hydrops. But it was astonishing to see how many low temperature curves were found. Most of the 51 cases of obstructive cholecystitis showed acute, advanced pathology and 14 of them were perforated, yet nearly half of these had maximum fevers of 99 degrees or less during their stay in the hospital before surgery was undertaken (Table VII) This study confirms our previous report and shows that the temperature curve cannot be relied upon

TABLE VI —QUALITATIVE FOOD DISTRESS

	Acute obstructive cholecystitis		Hydrops		Empyema	
	No.	%	No	%	No	%
None	6	60	5	25	1	8
Grade I	0		0		1	8
Grade II	3	30	5	25	1	8
Grade III	1	10	10	50	10	80
Belching						
None	4	40	7	44	0	
Grade I	2	20	0		1	7
Grade II	4	40	9	56	5	38
Grade III	0		0		7	54
Flatulence						
None	4	40	5	25	0	
Grade I	0		5	25	1	7
Grade II	6	60	5	25	10	79
Grade III	0		5	25	2	14

TABLE VII —HIGHEST TEMPERATURE

	Acute obstructive cholecystitis		Hydrops		Empyema	
	No	%	No	%	No	%
98 6	1	10	6	26	3	18
99	1	10	7	30	1	6
100	3	30	4	17	4	24
101	4	40	4	17	1	6
102	1	10	2	8	7	41
103	0		0		1	6

TABLE VIII —WHITE COUNT

	Acute obstructive cholecystitis		Hydrops		Empyema	
	No	%	No	%	No	%
6000	0		2	10	0	
7000	0		2	10	1	6
8000	2	20	2	10	1	6
9000	0		3	17	1	6
10000	1	10	2	10	0	
12000	1	10	4	21	4	22
15000	2	20	1	5	5	27
16000	2	20	1	5	1	7
21000	0		0		3	16
25000	1	10	0		2	12
30000	1	10	2	10	0	
Differential						
65	1	10	3	17	2	12
75	2	20	4	23	1	6
80	2	20	5	30	1	6
85	2	20	0		5	29
90	2	20	3	17	2	12
95	1	10	2	12	6	35

to determine the type or the stage of acute cholecystitis present Table VIII illustrates that the same observation holds true for the total polymorphonuclear and for the differential counts, for normal figures were obtained in a high percentage of cases In the majority of acute and subacute empyemas, both the total and differential white counts were high, but in the acute hydrops and the acute obstructive cholecystitis cases they were unreliably variable Attention has been called to the frequency of low white and differential counts in acute cholecystitis (4, 5), and this present study re-emphasizes this point. We have found the Schilling count of greater value than the total and differential white counts in acute cholecystitis

Jaundice had not been observed by any of the 10 patients who had acute obstructive cholecystitis and only 2 of the 24 who had hydrops had ever had icterus Neither of these groups had jaundice during the present illness Of the 17 patients having empyema, however, 6 were icteric while in the Hospital One had had jaundice 3 months previously during an attack of gall-stone colic, but no stones were found in the common duct at operation Of the 6 other patients who were jaundiced and had empyema, 4 had choledocholithiasis (Table IX)

Two important phases in the diagnosis and treatment of obstructive cholecystitis are illustrated in Table X The first shows the period in

TABLE IX —JAUNDICE

		%
Acute obstructive cholecystitis	None	
Hydrops	1 5 years ago	8
	1 After an abortion	
Empyema	3 While under observation	35
	1 Day of entrance	
	1 14 days after entrance	
	1 3 mos ago during a colic	

TABLE X.—PRE OPERATIVE PERIOD IN HOSPITAL

	Acute obstructive cholecystitis			Hydrops			Empyema		
Preop. period	No. cases	Not performed	Mortality and cause	No. cases	Not performed	Mortality and cause	Not [illegible]	Not performed	Mortality and cause
1 hour									1, peritonitis
12 hrs									
day				1					
days				1		[illegible]			
2 days	1		1, [illegible]						
day									
3 days				1					
4 days									
7 days							1		[illegible]
wks									1, [illegible]
3 wks									
5 wks					1	1, [illegible]	1		1, CD [illegible]
[illegible]									1 [illegible]
	14	1		14	1		17	1	5

the hospital before surgery was undertaken. The difficulty of determining the stage of the acute inflammation is graphically shown in the acute obstructive cholecystitis cases, for an almost equal distribution between early midway and late operation occurred. Some cases were considered acute and operated upon at once others were delayed days and even weeks before the lesion was considered surgical. In the hydrops and empyema cases, *however differentiation was easier* Most of the hydrops and some of the empyemas were operated upon early while a few of the hydrops and many of the empyemas were allowed "to subside" before operation was performed. The division in surgical attitude toward early or late attack in obstructive cholecystitis is clearly seen One of the 2 patients with perforated empyema operated upon immediately after entrance into the hospital but 5 days after the onset of acute symptoms, died on the second day after operation, *of peritonitis. Obviously this operation was* delayed too long by the patient. Another patient was operated upon 2 months after entering the hospital. He had had acute symptoms for 10 days before entering the hospital, and conservative treatment was instituted until the perforation walled off" Unfortunately however the gall bladder had not perforated but it did rupture while the surgeon was awaiting localization

The second feature illustrated in Table X, is the mortality and cause of death in relation to the time of operative intervention One of the 10 patients with acute obstructive cholecystitis, *operated upon on the fourth day died of pneumonia* 5 days later This might have been an avoidable death if operation had been done earlier Three perforations occurred in this group of 10 cases 2 patients were operated upon on the fourth day and one on the fourteenth day None died Perforation in acute obstructive cholecystitis is common and usually serious (1 3). Relatively little fibrosis is present in the gall-bladder walls and few adhesions are present around them Therefore the extravasations are widely disseminated *whenever perforation occurs* In the chronic obstructions (hydrops and empyema), *acute exacerbations are less likely to result in perforation* because of the extensive fibrosis of the gall-bladder wall. *If perforations do occur* they are more likely to develop slowly and to be walled off by neighborhood adhesions.

Three of the hydrops cases perforated, none of these died after operation. They were operated upon 1 2 and 4 days, respectively after entrance into the hospital. Two of the non-perforated hydrops patients died 1 operated upon on the

TABLE XI.—OPERATIVE PROCEDURE

Operation	Acute obstructive cholecystitis		Hydrops		Empyema	
	No.	%	No.	%	No.	%
Cholecystectomy		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Cholecystostomy			[illegible]	[illegible]	[illegible]	[illegible]

TABLE XII—PERFORATION OF THE GALL BLADDER

Pathology	Total cases	No perf	Day of op	Mortality and cause
Acute obstructive cholecystitis	10	3	4th 4th 11th	o o o
Hydrops	24	3	1st 2nd 4th	o o o
Empyema	17	6		
Acute	5	3	3 hr 4 hr 7th	o 2nd day peritonitis 7th day, embolus
Subacute	-	1	1st 35th	o 4th day CD stone
Chronic	10	2	2nd 2 mo	o 1 mo. ? cause
Acute exacerbation of chronic cholecystitis with stones	7	-	3 hr 2nd	o o
Subacute exacerbation of chronic cholecystitis	10	3	10 hr 8th 9th	o 3rd day myocarditis 6th day, ? cause
Typhoid fever		1	7 hr	o
Perforations operated before 2 days 9 cases				1 (11%)
Perforations operated after 2 days 9 cases				4 (44%)

second day, died after 8 weeks of abscesses of the brain, lungs, and liver The other, operated upon 5 weeks after entrance into the hospital, died in 12 hours from hemorrhage, blood oozing from all the gastro-intestinal mucosa

In the group of patients having empyema, 1 operated upon 2 weeks after entrance into the hospital, died on the sixth day after operation of pneumonia, and 1, operated upon 5 weeks after entrance, died on the fourth day of an overlooked stone in the common duct Five perforations were met with in the 17 patients having empyema of the gall bladder Two of these were operated upon within 3 hours after entering the hospital, 1 of the 2 died of peritonitis on the second day after operation The peritonitis was present at the time of operation, and it is problematical whether delayed surgery might have circumvented this death Two patients with perforated empyemas, operated 1 and 8 weeks, respectively, after entrance, died on the seventh day of embolus and on the thirtieth day of an unknown cause (no autopsy) In 1 of these cases operation was delayed, to permit the perforation to wall off Earlier operation might have been life-saving The fifth perforated empyema was operated upon 3 weeks after entrance into the hospital, he made an uneventful convalescence When to operate, early or late, is a decision that must be based on sound surgical judgment (2, 6, 7, 8) In these groups of obstructive cholecystitis cases, the mortality was less in those operated upon early When Table XII is consulted, it is seen that the balance is decidedly in favor of earlier operation, for of 9 patients with perforated cholecystitis operated upon within 48 hours after entrance into the hospital, the mortality was 11 per cent in contrast to 44 per cent mortality in the 9 patients operated upon after 2 days

The pre-operative diagnoses made in the present series of 51 cases of obstructive cholecystitis illustrate again our difficulties in correctly delineating the differential pathology in acute cholecystitis But because of these difficulties, we have tended to circumvent the task of defining the detailed pathology by classifying all the acute lesions as "acute cholecystitis" One of the purposes of this essay is the desire to encourage a differential diagnosis, particularly between obstructed and non-obstructed lesions in acute cholecystitis Practically all of our cases were diagnosed acute cholecystitis, but very few were given detailed and more specific diagnoses (Table I) An accurate pre-operative diagnosis was avoided in this way, the surgeon lost the opportunity to improve his diagnostic acumen and the patient was handicapped by the indefinite diagnosis for the advisability of early or late operation was not indicated That we are more conscious of the complications of acute cholecystitis, however, is seen in the 5 instances of erroneously diagnosed perforations Most of these patients were subjected to early surgery, and all without mortality

For follow-up studies, a detailed description of the pathological condition encountered at operation is necessary. The surgeon has the first and best opportunity to depict the pathological process. When the removed specimen is examined in the pathological laboratory its contents are often missing, due to the study of the opened specimen in the operating room. Little bile, pus, or white bile accompanies the gall bladder into the laboratory and so the pathologist is deprived of this diagnostic aid. As a result, the surgical and pathological diagnoses differed in many of our cases. I believe the contents of the gall bladder offer the safest guide in defining the pathological process in obstructive cholecystitis. As long as there is bile in the gall-bladder cavity and regardless of how much pus is mixed with the bile, this type of obstructed gall bladder should be called an acute obstructive cholecystitis. As long as white bile (mucus) is found, regardless of the amount of pus that may be mixed with it, the specimen is a hydrops either acute, subacute, or chronic, depending on the amount of inflammation present. The term "empyema" I reserve for the gall bladder that contains only pus.

Most of the operations performed on the 51 cases of obstructive cholecystitis were cholecystectomies, but an unduly high percentage, in my opinion, were cholecystostomies (Table VI). Simple drainage was preferred in 35 per cent of the cases by the 6 surgeons concerned in this review. Cholecystostomy is often the operation of choice, particularly in the aged, debilitated, and very ill, but when done, it should be remembered that a second operation, cholecystectomy, will probably be necessary. Of the 51 cases of obstructive cholecystitis 8 (15 per cent) died, 6 of which were perforated. About 50 per cent of this mortality is due to late surgery. The operative method is also important, however, for in this study 66 per cent of the patients having a cholecystostomy for acute cholecystitis died, while only 7 per cent of those having cholecystectomy died. One might conclude that only the very ill were subjected to cholecystostomy. But 7 patients having perforations were treated by cholecystectomy without fatality, while 3 of 6 patients with perforations treated by cholecystostomy died. One of 3 patients having a cholecystostomy but only 1 of 13 patients having a cholecystectomy for acute hydrops died.

The method and the application of the method are important considerations in the surgical treatment of acute cholecystitis. My own preference is for excision whenever possible. It can usually be done and without dispersion of the acute infection, if adherent omentum is excised with the specimen. I have regretted performing cholecystostomy more often than I have regretted performing cholecystectomy in acute cholecystitis.

CONCLUSIONS

1. The pathology of acute obstructive cholecystitis is progressive, empyema being the eventual outcome.

2. The mortality in the treatment of acute cholecystitis will be decreased if the obstructive lesions are differentiated, clinically, from the non-obstructive.

3. Perforations of the most serious nature occur most frequently in acute obstructive cholecystitis. All of our mortality in perforations, however, occurred in the subacute perforations (into a walled-off area) for the clinical signs did not indicate what was brewing. Surgical intervention was therefore delayed too long.

4. Acute cholecystitis that cannot be differentiated clinically should be operated upon within 4 to 48 hours after the patient enters the hospital.

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PREGNANCY FOLLOWING CESAREAN SECTION

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THERE have been numerous articles written on the subject of pregnancy following cesarean section and especially on the dictum, "Once a cesarean always a cesarean" There is some divergence of opinion as to the truth of this dictum, although the weight of evidence is against it. The basis of this paper is a statistical study of the cases of pregnancy following cesarean section that have been under the care of the Woman's Clinic (indoor service) of the New York Hospital for the first 25 months from the date of its opening, September 1, 1932

During this period of time there were 5,353 full term and premature deliveries and 319 abortions on the indoor service Of these 5,672 cases there were 92 patients, or 1 62 per cent, who had been previously delivered by cesarean section, and it is this group that will be considered in detail

Of these 92 patients 46 were again delivered by cesarean section, while 24 delivered spontaneously, 15 had an operative delivery other than cesarean section, and 7 patients had abortions Therefore, in this group of 92 pregnancies following cesarean section 85 of the patients had a full term or premature delivery Of these 85 patients 46, or 54 12 per cent, were delivered by section Delivery through the normal birth canal, either spontaneous or operative, occurred in 39 of the 85 cases, or 45 88 per cent. The total number of cesarean sections in the clinic during this 25 month period was 157, or an incidence of 2 93 per cent. Of these 157 sections 46, or 29 92 per cent, were done in patients who had had a previous section

These 92 patients, who had been previously delivered by cesarean section, will be considered under the following headings which are based upon the type of delivery in this present pregnancy

I Abortion cases
II Full term and premature delivery cases
  1 Vaginal delivery
    a Operative
    b Spontaneous
  2 Cesarean section

I ABORTION CASES

A study of the group of patients in whom the present pregnancy ended in abortion will be considered separately The indications for the previous sections in these cases had been as follows

	Cases
Eclampsia	1
Contracted pelvis	4
Large infant	1
Ruptured uterus after a previous cesarean section for premature separation of the placenta	1
Total	7

One patient in this group had had two full term deliveries (1 delivery by forceps and 1 by version and extraction) following 3 classical cesarean sections The indications for these sections had been, for the first, premature separation of the placenta, for the second, ruptured uterus, and for the third, previous cesarean section In only 3 instances were the abortions spontaneous, and of these, 2 were admitted to the hospital later because of vaginal bleeding and a curettage was done to complete the abortion. Table I shows the type of operative procedure in this group, and the indications for interference with the pregnancy

TABLE I —TYPE OF OPERATION

Cases	Duration of the pregnancy	Type of operation	Indication
1	3 months	Subtotal hysterectomy	Chronic nephritis
1	3 months	Subtotal hysterectomy	Chronic valvular heart disease
1	3½ months (twins)	Abdominal hysterotomy	Vomiting of pregnancy
2	2 and 4 months	Dilatation and curettage	Incomplete spontaneous abortion
1	2 months	Dilatation and curettage left salpingectomy	Ruptured tubal pregnancy

II FULL TERM AND PREMATURE DELIVERY CASES

In the remaining 85 cases only 3 were premature deliveries and of these 2 were spontaneous and 1 operative. These 3 premature deliveries are included in Tables II, III, and IV

TABLE II.—RACE DISTRIBUTION

Type of delivery	Race White	Race Colored	Total
Spontaneous	17	7	24
Vaginal operative	14	1	15
Cesarean section	34	12	46
Total	65	20	85

TABLE III.—AGE DISTRIBUTION

Years	Type of delivery			Total
	Spontaneous	Vaginal operative	Cesarean section	
—19		1		
20—24	8			14
25—29	3		1	19
30—34	4	6	16	42
35—39	1	1	1	13
40+				3
Total	54	73	46	93

The types of pelves as classified at the time of discharge from this hospital following delivery are shown in Table IV

TABLE IV.—TYPES OF PELVES

Pelvis	Type of delivery			Total
	Spontaneous	Vaginal operative	Cesarean section	
Normal	5	11		37
Simple flat			13	37
Generally contracted typical	3			24
Generally contracted formal			6	6
Kyphotic				
Flat formal			1	1
Rhachitic, generally contracted				
Rhachitic, flat				
Pelvis typical				
Total	54	1	46	93

In the spontaneous delivery group 62.50 per cent had normal pelves in the operative vaginal group 73.33 per cent in the combined group of cases delivered through the normal birth canal 66.66 per cent had normal pelves, while in the group of cases having the present pregnancy terminated by section the incidence of normal pelves was 23.91 per cent

Vaginal deliveries There were 39 deliveries through the normal birth canal The presentations are given in Table V

One patient in the group having a spontaneous delivery and 1 in the group having an operative delivery had had two previous sections The types of section just preceding the present delivery are shown in Table VII

TABLE V.—PRESENTATION

Presentation	Type of delivery		Total
	Spontaneous	Operative	
L.O.A.	14		18
L.O.T.			1
L.O.P.			
R.O.A.	7	4	
R.O.T.			3
R.O.P.			
L.R.A.			
R.R.A.			

TABLE VI.—DURATION OF LABOR

Hours	First stage		Minutes	Second stage	
	Type of delivery			Type of delivery	
	Spontaneous	Operative		Spontaneous	Operative
1—6	14	1	1—19	19	
7—12	7	6	20—39	13	4
13—18			40—59		4
19—24			60+		6
25—30					
31—36					
37—42					
43—48					
Unknown		9			

TABLE VII.—TYPE OF SECTION

Type per cesarean section	Type of delivery of present pregnancy		Total
	Spontaneous	Operative vaginal	
Classical		5	16
Low cervical	6	3	
Lateral			1
Unknown	6	5	
Total	54	14	31

The indications for the previous cesarean section as obtained from the patient and when possible from the record of the previous history are given in Table VIII

The puerperium following previous cesarean section was febrile in 11 instances, no record could be obtained in 17 cases, and the remainder of 11 were normal At the time of the present delivery a description of the scar resulting from

TABLE VIII —INDICATIONS OF PREVIOUS CESAREAN SECTIONS

Contracted pelvis—(It is of interest to note that at the time of discharge from this hospital following delivery 8 pelves of this group were classed as normal)	14
Placenta previa	6
Premature separation of placenta	1
Prolonged labor, no progress	3
Large infant	2
Eclampsia	1
Cervical dystocia	1
Bandl's contraction ring	1
Other as breech, vesicovaginal fistula, ovarian cyst	4
Unknown	6
Total	39

the previous section was noted infrequently, in the operative vaginal delivery group a slight longitudinal defect was noted in 1 case and a fascial defect in another, in the spontaneous delivery group a thin lower uterine segment was described in 1 case and a depression in the uterine scar was felt in 2 instances In this group of 39 cases since the last cesarean section and before the present delivery, 4 patients had a spontaneous abortion (1 later had a forceps delivery), 3 a spontaneous delivery, and 3 a low forceps delivery

a Operative vaginal In the operative vaginal cases the types of operations are given in Table IX

TABLE IX —TYPES OF OPERATION

Low forceps	8
Mid forceps	3
Breech extraction	2
Induction of labor by insertion of Voorhees bag	1
Manual removal of placenta	1
Total	15

(There were 2 postpartum hemorrhages, one 600 cubic centimeters, the other 2,200 cubic centimeters.)

The indications for the forceps deliveries are shown in Table X

TABLE X —INDICATIONS FOR FORCEPS DELIVERY

Contracted pelvis, previous section	4
Prolonged second stage of labor	2
Fetal distress	5
Total	11

The induction of labor by insertion of a Voorhees bag was done because of pre-eclampsia, the patient having had a previous cesarean section for eclampsia One patient in this group of 15 had a bicornuate uterus and 2 others had a toxemia (low reserve kidney)

b Spontaneous In the spontaneous group of 24 cases there were 5 patients with toxemia (3 had a low reserve kidney, 2 an unclassified toxemia), and 2 had a positive Wassermann reaction

Summary of vaginal delivery cases There were no maternal deaths in this group of 39 patients There was 1 infantile death, a deadborn macerated fetus weighing 1860 grams, length 43 centimeters, Wassermann reaction negative, delivered spontaneously, mother had a toxemia (low reserve kidney)

The weights of the infants in this group are given in Table XI

TABLE XI —WEIGHT OF INFANT

Weight	Spontaneous	Operative	Total
—2500 gm	2		2
2500—2999	5	1	6
3000—3499	14	7	21
3500—3999	2	5	7
4000+	1	2	3
Total	24	15	39

2 Cesarean section Of the 92 who had a previous cesarean section, 46 patients were again delivered by cesarean section Of this number 11 were given a trial of labor varying from 9 to 13 hours before operation was decided upon Fourteen patients had had 2 previous cesarean sections, 1 patient had had 3 low cervical sections, and another had had 4 classical sections

Table XII enumerates the types of sections just preceding the present delivery and Table XIII gives the indications for these operations

TABLE XII —TYPE OF SECTION JUST BEFORE PRESENT DELIVERY

Classical	10
Low cervical	21
Latzko	3
Unknown	12
Total	46

TABLE XIII —INDICATION FOR PREVIOUS SECTION

Contracted pelvis—(at the time of discharge from this hospital following delivery 3 of these pelves were classified as normal)	31
Prolonged labor, no progress	3
Placenta previa	1
Three deadborn infants	2
Previous section, febrile puerperium	2
Large infant	1
Twins	1
Unknown	5
Total	46

The puerperium following the previous cesarean section was febrile in 18 cases, normal in 10 cases and unknown in 18

Table XIV gives the indications for the present cesarean sections.

TABLE XIV.—INDICATION PRESENT OPERATION

Contracted pelvis	32
Defective uterine scar (afebrile puerperium)	5
Defective uterine scar (previous febrile puerperium)	6
Ruptured uterus	1
Disproportion	1
Previous cesarean section (diabetes)	1
Total	46

Cesarean section scar. The scar of the previous operation was not described in 30 cases during the antepartum or intrapartum period. The descriptions of the scars of the other cases were definite depression felt, defect in upper angle of scar; evidence of old infection; thin abdominal scar; keloid adherent to anterior surface of uterus, and defect in uterus. At the time of the present operation, no mention was made of the conditions found as an end-result of the previous operation in 13 cases. The descriptions of the others showed no adhesions in 4; no uterine scar in 1; omental adhesions in 7; many adhesions in 15; uterine scar in 4; 1 ruptured uterine scar opening 18 by 12 centimeters.

Vaginal delivery between the abdominal deliveries. There were 10 patients who had vaginal deliveries during the period between their previous and present abdominal deliveries. These vaginal deliveries are tabulated in Table XV.

The types of cesarean section in the present delivery are shown in Table XVI.

TABLE XVI.—TYPE OF PRESENT SECTION

Classical	38
Low cervical	7
Latzko	1
Radical (ruptured uterus)	1
Total	46

Anesthesia. The anesthesia used in 44 cases was nitrous gas, oxygen and ether. The 2 other sections were done under local anesthesia, and a small amount of gas oxygen was also administered.

Rupture of membranes. The time of rupture of the membranes is shown in Table XVII.

TABLE XVII.—TIME OF RUPTURE

Membranes ruptured at time of operation	32
Membranes ruptured 1 to 4 hours before operation	3
Membranes ruptured 5 to 9 hours before operation	1
Membranes ruptured 10 to 14 hours before operation	1
Membranes ruptured 15 to 20 hours before operation	2
No record	7
Total	46

Puerperium. The puerperium was normal in 14 cases, febrile in 11, and there was a one day fever in 16 cases. In only 1 of the 11 patients having puerperal infection did the membranes rupture before operation and in this instance rupture occurred 5 hours previous to operation. Three patients in this febrile group had a trial labor of 9, 12 and 17 hours, respectively. Six of the wounds

TABLE XV.—INTERVENING VAGINAL DELIVERIES

Case No.	Previous cesarean section		Vaginal delivery	Present cesarean section	
	Number and type	Indication	Type	Type	Indication
	Unknown	Large infant	Spontaneous abortion	Classical	Previous uterine hysterectomy
	Classical	Flat pelvis	Spontaneous abortion	Classical	Simple flat pelvis
3	Low cervical; 1 Unknown	Generally contracted rhachitic pelvis	Spontaneous abortion	Classical	Generally contracted rhachitic pelvis
	Low cervical	Flat pelvis	Spontaneous abortion	Classical	Previous uterine febrile puerperium
5	Low cervical	Flat pelvis	Spontaneous abortion	Classical	Simple flat pelvis
6	Low cervical	Flat pelvis	Spontaneous abortion after first section	Low cervical	Simple flat pelvis
7	Low cervical	Unknown	Spontaneous abortion after first section	Classical	Generally contracted flat pelvis
8	1 Unknown	Flat pelvis	Full term spontaneous delivery after first section	Classical	Generally contracted spinal pelvis
9	Low cervical	Placenta previa	Full term spontaneous delivery	Classical	Generally contracted spinal pelvis
10	Latzko	Third pregnancy. No living child	Full term forceps delivery	Classical	Simple flat pelvis

had superficial suppuration, 3 occurring in the febrile group, the others in the patients with a 1 day fever In only 1 of the 6 cases did the patient have a trial of labor, 12 hours, and in every instance the membranes ruptured at the time of operation Sterile vaginal examination was done in 7 patients, 2 of whom had a febrile puerperium and of these 1 had a wound infection Two patients in the 1 day fever group had questionable massive collapse of the lung One patient in the afebrile group developed a puerperal psychosis

Maternal mortality There was 1 maternal death The patient was a colored woman, aged 40 years, gravida 4, pelvis normal, had 1 previous classical cesarean section because of a large infant, 1 spontaneous abortion after this, and was delivered by classical cesarean section in this pregnancy, the indication being a previous section, type of puerperium unknown The patient also had diabetes for which she was receiving treatment. Following the section the patient had a postpartum hemorrhage and died a few hours after the operation not having responded to tamponade of the uterus and medication Autopsy finding was thrombosis of the ovarian veins

Sterilization Tubal sterilization was performed in 15 cases

The indications for sterilization were as in Table XVIII

TABLE XVIII —INDICATION FOR STERILIZATION

3 sections, ventral hernia repaired at time of last section	1
4 sections, ventral hernia repaired at time of last section, toxemia (low reserve kidney)	1
3 sections, ruptured uterus	1
3 sections, old hemiplegia	1
2 or more sections	11
Total	15

One patient received contraceptive advice following the second section

Infantile mortality Infantile mortality includes all stillborn or deadborn infants, and all neonatal deaths occurring in the first 14 days of life.

There were 5 infantile deaths in the group of 46 patients having cesarean section These are shown in Table XIX.

TABLE XIX —INFANTILE DEATHS

Deadborn infant—mother admitted with ruptured uterus
Deadborn infant—asphyxia
Infant died second day—pleural and pericardial effusion
Infant died second day—atlectasis
Infant died fourth day—icterus gravis

The distribution of the weights of the infants is given in Table XX

TABLE XX —WEIGHT

Weight in grams	No of infants
—2500	1
2500—2999	7
3000—3499	21
3500—3999	14
4000—4499	2
4500+	1
Total	46

CONCLUSIONS

1 In a group of 92 pregnancies following cesarean section 7, or 7 61 per cent, resulted in abortions

2 The maternal mortality in the entire group was 1 in 92 cases, or 1 086 per cent. This death occurred in the group of 46 patients in whom the present pregnancy was terminated by cesarean section

3 The infantile mortality in the entire group was 6 deaths in 85 cases, or 7 058 per cent There were 5 infantile deaths in the 46 cases again delivered by cesarean section, an incidence of 10 869 per cent.

4 Delivery through the normal birth canal following a previous cesarean section occurred in 45 88 per cent of the patients with good results in the case of the mother and in all but 1 infant.

5 The fact that a patient has had one cesarean section does not indicate that she must be delivered by section in a future pregnancy unless some abnormal condition exists The previous section may have been done, for example, because of premature separation of a normally implanted placenta In every case the patient should be carefully studied during the succeeding antenatal period, admitted to the hospital for observation a few days before the expected date of delivery, and closely watched during labor A thin uterine scar, a defect in the uterine musculature, or a history of a febrile puerperium following the previous section may be indications for another cesarean section, depending upon the conditions noted after careful study and observation of the patient

6 This study reveals the importance of having recorded in the histories accurate pelvic measurements, detailed descriptions of the indications for, and the type of, operation performed, and the patient's course during the puerperium Cooperation between hospitals is necessary so that abstracts of the patient's record may be easily obtained by the clinic or doctor caring for the patient in a future pregnancy Proper intelligent care and treatment cannot be given the patient unless such facts are known

AMPUTATION OF THE FINGERS

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No apology is needed for discussing a subject considered by many surgeons of minor importance. Indeed, it would seem that more care of and attention to conditions affecting the function of the fingers should be urged upon all surgeons.

Fingers, when lost are irreplaceable. There are no satisfactory substitutes, no adequate artificial appliances to take their places. The hand is an organ perfected to the highest degree as to the functional organization of its structures. Its tendons, muscles, nerves and blood vessels, its fascias, joints and bony parts are all combined to produce a marvel of architecture and engineering not equalled in any other structure of the body. The ultimate purpose of the entire appendage from the shoulder down is to endow the fingers with the greatest possible flexibility and sensitiveness for the performance of individual and co-ordinated movements, from the simplest to the most complex, with great speed, facility and minute accuracy.

The fingers are the end organs of the arm. Their sensory parts carry soft but firm pads; their tendons are encased in perfectly fitting sheaths; their tips are shielded by semi-rigid nails; their joints are stabilized by a complicated system of ligamentous bands; and last but not least, their nerve supply is multiple, so after the destruction of one nerve a measure of function may remain.

A hand without a thumb lacks about half its usefulness. A hand without index finger and thumb is nearly useless. Even the smallest portion of the distal phalanx lost from the tip of any finger constitutes a lamentable loss to trained hands. It is, therefore, increasingly desirable to use all possible skill when faced with the problem of preserving or reconstructing crushed fingers.

The goal of all amputations is the production of a useful stump. Useful in the case of fingers, means retained length, conservation of movements, and preservation of as many of the special sensory end organs in the skin and the pulpy tissues of the flexor surface as possible. A single finger or adequate stump of finger capable of some movements and function is better than an artificial hand. Another consideration, especially in traumatic injuries, is the prevention of infection. A superveniting infection can vitiate the most promising work of repair.

In preparing a finger for operation, cleansing of the hand of grease and dirt should be done in the usual way. An antiseptic may be applied to the skin up to the area crushed, but not to the wound itself. Then the finger to be amputated is draped with a towel so that all the remaining fingers are carefully and completely covered. Figure 1 illustrates this method. Thus the chances for infection by contamination are reduced.

Amputation through the distal phalanx may often be avoided by transferring a full thickness skin graft from the thigh and covering the severed end, particularly when the injury consists of a severance by a sharp instrument or cutting tool. Another method which is occasionally found successful, especially when the cut is through the nail, is a plastic bridge flap from the finger itself (Fig. 2). A small incision is made across the front of the finger a short distance from the severed end, and then the tissue is drawn over the end of the stump and sutured skin to skin. The resulting defect is then immediately covered by a

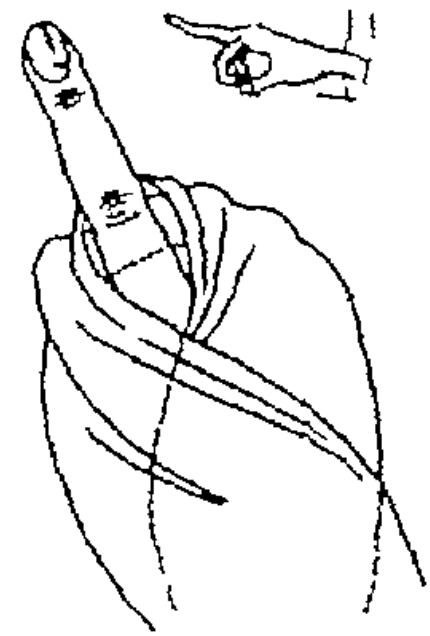

Fig. 1. Method of draping the finger for operation. The hand is placed upon a sterilized towel in the manner shown in the insert. The towel is folded back leaving the finger but covering all the other parts of the hand and wrist when it is folded over the back of the hand.

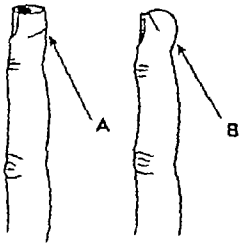

Fig 2 Method of repairing the tip of a finger by plastic bridge flap *A*, skin incision partly encircling the finger *B*, Plastic flap drawn over the end of the stump, covering the tip, but leaving a small skin defect at the point of the arrow The defect is covered with a skin graft.

thin graft Such repair has the advantage of placing an adequate pad over the end of the bone and of preserving the stump to its fullest possible length

Crushing injuries of the fingers usually occur during work, when the patient's hands are more or less dirty Such an injury is almost sure to become infected unless certain essential precautions are taken Not only may the injured part become infected, but the entire hand, after amputation, is likewise exposed to infection It is of prime importance to do the necessary amputation just as soon as possible after the injury One should never wait until the following day The infection may enter the lymphatics and proceed toward the hand in a few hours Early amputation often avoids this

Equally important is the method of operation Under no circumstances is any undercutting or upward dissection of the crushed tissues done The finger is prepared for operation in the usual way and a tourniquet applied around its base Then a large cutting needle is passed through the torn tip once or twice, carrying a heavy silk worm gut suture This is not tied, but a forceps clamp is applied to it so that secure traction can be made distally in the long axis of the finger (Fig 3*A*) By this means the part to be amputated is at all times under control, is easily and accurately handled, and at no time has the surgeon any need to touch the contaminated crushed tissues with his gloves, nor any instrument except the needle which is immediately discarded Instead of the large suture a towel clip may be used for the same purpose An assistant holds and handles the suture in such a way that there is no contact between the crushed finger and any of the other things involved in the operation, thus avoiding contamination and subsequent infection

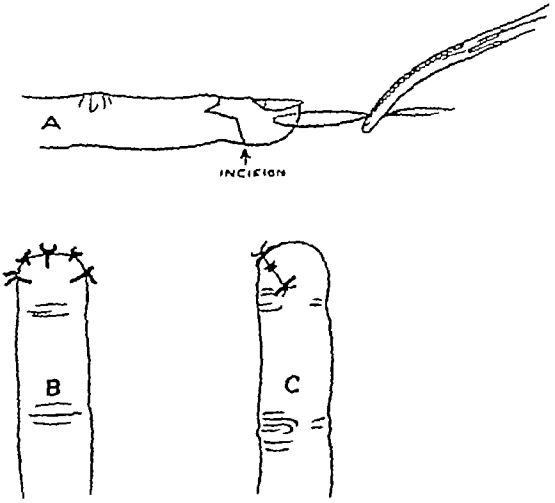

Fig 3 Method of amputating the distal phalanx *A*, Suture passed through the crushed tissues for traction and control, lines of incisions Note slight bevel of the dorsal and volar incisions, and the notch joining the two incisions on the side. *B*, Suture of the stump Note particularly the deep central suture, which is placed first, and the two deep lateral sutures, which must include the digital arteries and are, therefore, directed laterally Note also the two superficial coapting sutures *C*, Side view of sutured stump Note position of the suture line well back on the tip of the stump, and the adequate soft pad over the end

In doing the actual amputation the finger is pulled out straight and the knife is placed squarely across it on the flexor surface, just 1 millimeter proximal to the torn tissue, and then a single cut is made down to the bone, slightly slanting proximally (see Fig 3*A*) Thus the knife will pass only through healthy tissue, leaving all the crushed portion distally Then the dorsal cut is made in the same way, but its flap is made shorter by about one-third the thickness of the finger This is for the purpose of allowing the volar flap to extend over the end of the stump The ideal flaps are of such length and pattern that the line of union will curve across the end in the same position where normally the finger tip joins the finger nail (Fig 3*C*) Both of these cuts are made straight across and slanting only slightly proximally, no attempt whatever being made to encircle the finger The volar incision will be considerably deeper since the bony phalanx lies close under the dorsal surface This will give the proper relation between the two flaps as to length and thickness The two flap incisions are then joined on the two sides by small notches, one on each side, cut as outlined in Fig 3*A*

Each of these incisions should be made cleanly with a single application of the knife so that all of the soft tissues will be divided and the bone exposed, ready for cutting across with the bone forceps. This is done high up in the incisions but undercutting is not necessary. The cut end of the bone must be smooth, and if spicules are present they should be carefully removed.

Closure of the flaps is simple. The sutures may be dermal fine silk or fine silkworm gut. The first suture is placed in the center quite deeply then one suture is placed on each side so as to close the notch which was cut to join the dorsal and volar incisions, as indicated in Figure 3*B*. Two superficial coapting sutures finish the closure. No catgut is used since the vessels are caught in the two deep lateral sutures if they have been placed properly and carried deep enough to include the digital arteries. Hemostasis will be complete and healing will be by first intention. The stump will be smooth rounded and well padded, and the line of union of the flaps will be an inconspicuous scar well back on the tip of the stump.

If the line of amputation is through one of the interphalangeal joints, the skin incisions are exactly the same after which the joint cavity is opened on the dorsum with the knife when the distal part has been placed in flexion. In this way the joint cavity is easily located and the process is made easy to perform.

Tendons in the fingers have their attachments at the bases of the bony phalanges. By saving the base of the middle phalanx the attachment of the sublimis tendon is preserved. And by saving a portion at the base of the distal phalanx, the attachment of the profundus tendon is left intact. Disarticulation through the proximal interphalangeal joint as well as severance through the proximal phalanx will leave the stump without tendon control. This should be avoided if possible.

Disarticulation through the metacarpophalangeal joint is followed by an unsightly result. This is to be preferred, however to resection of any part of the metacarpal bone. The usefulness of the palm of the hand is greatly dependent upon the integrity of the normal relationships of the heads of all the metacarpals. The removal of a metacarpal, or even a portion of its head is bound to interfere greatly with the function of the hand.

SUMMARY

A technique for amputation of the fingers is described which aims at reduction of infections and the formation of a useful stump.

EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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1905–1935

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MAY, 1936

CHARLES JEFFERSON MILLER

IT is with profound regret that SURGERY, GYNECOLOGY AND OBSTETRICS records the recent death of one of our country's great surgeons, Dr C Jeff Miller, a regent of the American College of Surgeons and past president, 1930-1931

Long a leading figure in American gynecology, a fellow and officer of the American College of Surgeons, the American Gynecological Society, American Medical Association, and member of many other national and local medical and surgical societies, he lent dignity to them all As professor of gynecology at the Medical School of Tulane University and Touro Infirmary at New Orleans he exerted a profound influence on the surgery of the South and was recognized as one of its most able exponents A native of Tennessee, his Southern culture, courteous manner, and philosophic attitude surrounded him with hosts of friends who admired him and loved him To his family the Editorial Staff of the Journal extends its deepest sympathy

SURGERY, SPECIALTY SURGERY, AND "PLASTIC" SURGERY

THE term "general" as applied to a surgeon indicates neither the quality of his work nor the extent of his endeavors, but implies a basic grasp of medical and surgical principles that permits development along any chosen line of practice, as well as a dominant concern for the activities and the well-being of the body as a living unit and for its subjective functions Because the machinery of these vitalizing subjective functions is housed in the cavities and in the peripheral bulk of the whole body, the devotees were called "general surgeons," in distinction to the on-coming specialist who is more interested in one or more objective functions such as sight, hearing, locomotion, reproduction, esthetic appeal etc However, all body-parts and functions are so interdependent in action and being that in their care independent fields of practice cannot obtain The buccal mucosa, the eye, or the larynx may first manifest symptoms characteristic of a distant lesion, and the otolaryngologist, for instance, assumes responsibility in commonly occurring infections prone to extension into the cranial cavity, the lungs, or the blood stream

Breadth of vision is essential to good practice in any field and is fostered by broad study, broad opportunity, and broad observation Concurrently these also foster realization of the value of concentrated effort, and in this realization all specialization has its inception All surgical specialties rest upon fundamental principles that were guiding formulas to the older surgeons and still are to those of the present day

It may be advanced even while lacking statistical confirmation that there is more effective specialization practiced within than outside the general surgical field, for few if any responsible surgeons will today claim to do well all kinds of surgery in all parts of the body One of the most widely useful instances, and a common one is the surgeon who treats only the more ordinary affections, but in nearly all parts of the body He who limits his care to any and all affections of certain individual structures or geographic areas is another example of a general surgical specialization and a third is he who does a particular type of surgery, or treats a particular type of disease, deformity or injury in one, any or all areas.

These are instances of discretionary self limitation which, in practice, averages less sharply defined than when it is a mandate of a conventionalized specialty The earlier concentration in effort that has become the accepted procedure of the latter begets a greater exactitude which is compensatory just so long as the purpose and scope of this or that particular limited training is adhered to. However in all lines of surgical endeavor a few men will show a flair for outstanding constructive work, and in certain fields the results may be so striking as to bring a disproportionate return in recognition and opportunity Then, unless this exaggerated confidence is met with honesty and sound judgment, disappointment or disaster may ensue Such sequences are not unknown in connection with the so called new overpublicized and often half-baked plastic surgery which, as a specialty concerns itself chiefly with surface and contour confines its activities to no particular area, and to which none of the segregated specialties can substantiate proprietary rights. It does conserve chiefly the objective functions, sight, hearing, ease of movement, reproduction esthetic appeal, etc., but it is also directly or indirectly applicable to many of the subjective functions. The basic factors which influence healing are the same in all types of surgery and, except for simple ligations, incisions, and guillotine amputations, the transfer and molding of the tissues are an essential part of nearly all surgical operations. Further as many of the steps may tax the subjective functions to the limit of endurance this surgery can be best and most safely done only when shepherded by all possible precautions that surgery can provide. The title "contour surgery" would be more individualistic, but our analysis is not given to provoke controversy over an accepted name but rather to accentuate the relation of this specialty to the whole surgical scheme, and that when practiced on a broad scale it should again be classed as a general surgical specialty Orphaned in the passing of the older surgery later recognition was long withheld, owing partly to the distractions incident to the establishment of the aseptic era, and to a greater degree to the persistence of a very old and deep-rooted prejudice of the surgeon against prostituting his art to esthetic appeal. It took a World War to awaken a rather unprepared profession to the need of and the opportunity for this work being well performed This war need was partly met by a few general surgeons who had previously fancied this work, but chiefly by individuals from among the rhinologists, the gynecologists and the oral surgeons whose more exacting technical habit made a convenient foundation upon which to build. Working in close association with the general teams they quickly learned to spread their gift widely and have remained outstanding figures in post-war civilian practice.

In spite of later conscientious efforts to give on-coming aspirants this necessary double

training, no widely applicable and satisfactory plan has yet been emphasized There is necessarily something approaching a gift back of its higher flights which cannot artificially be called into being and without a natural flair the work cannot go beyond standardized mediocrity Given the combination of ability and the will-to-do, both quality and facility of production can be stepped up indefinitely by training and circumstance

Can we not, in controllable civilian practice, duplicate the features that proved productive in the haphazard of war surgery? There is the same need with also the same material, and equally appropriate circumstances an increasing multitude demanding surgery that might better their social, business, or industrial circumstances And there are surgeons anxious to meet this need, and everywhere highly organized surgical services in which opportunity and non-hampering guidance could be given with mutual profit The first essential is the choice of material and in this the ring of the metal not the mold in which it has been cast should be the chief guide

Next in importance is maintenance of close and mutually satisfactory working co-operation both with the general surgeons and the other surgical specialists This association will also widen the potential sources of future practice It is particularly important in those borderline cases which overlap—the no-man's land frequently lying between more conventionalized spheres of practice, where the patient may become the victim either of unconscious neglect or misdirected enthusiasm Thirty-six per cent of the cases coming to our own service last year could have been ticketed as surgical junk as the result of our own or the other man's lack of foresight in planning or execution, or both Group co-operation begets a surgical spirit, and the latter is somewhat adverse to the habit of sequestered operating, especially by those who avail themselves of the opportunity of other clinics

Some, by choice, work on very narrow lines, their success depending upon personality, skill, salesmanship, and reputation Quite a number do this as routine work in a special field, but for the on-coming the greatest opportunity will be for those who are prepared to do the work in any area For the otherwise qualified man, limited in basic surgical training and experience nothing can give more comfort and safety in a gradually expanding field than the co-operation of a trained house staff The latter should also prove the most fruitful source from which to choose the associate who is to extend the number of his productive years, and the wise man will do this before his utility becomes but a name If he waits until he has only his place to give, then he cannot complain should the associate show anxiety to replace him Reading, personal experience, and clinic visiting will register in the long run, but acquired academic degrees bring nothing more than entrée to these training camps, for operative surgery is essentially a postgraduate study

To be productive this staff assignment must be a consistent fact, not merely nominal, and, even while developing, the encumbent must eat, and might aspire to rearing a family An empty stomach is a great urge to industry but may tend to lower quality, therefore, some sort of provision for maintenance might not only be helpful but necessary

There has been a disposition to relegate this work to housemen or to those considered not quite equal to making good on real surgery, or to regard it as purely a matter of technique, either of which is unfortunate While most surgery gets by on functional results, this must stand or fall not only upon its approximation of normal or ideal surface

and contour but also upon comprising a psychology that may be most difficult either to interpret or to satisfy The casual request for this or that may be a timid expression of the deepest of heartfelt desire. Usually our best is none too good and often the very best could not really satisfy

In spite of the above, the effort is usually well worth while, if we evaluate results in terms of remunerative employment restored self-confidence, and of greater accomplishment in terms of compensation and liability expenditures and in terms of better health and of happiness to be won through surgery

VIRGIL P BLAIR.

VAGINAL HEAT TREATMENT OF PELVIC INFECTIONS

THE application of heat as a means of treating infections of the pelvic viscera of women is recognized as a useful therapeutic procedure. In 1931 appeared the report of the use of a heat regulating machine designed by Elliott This was received with considerable enthusiasm and the method was given a trial by many individuals and institutions. Attention was drawn in the lay press to the use of this apparatus and the general impression seemed to be that an agent had at last been found to cure all infections peculiar to the female genital tract. Experience has naturally proved this to be untrue With this realization it may be that a reaction against this method of therapy has set in

A sincere effort has been made to evaluate accurately the position of this apparatus in gynecological practice As has been stated elsewhere regardless of the source of heat, the general rules of treatment of pelvic infections of women have not been altered by any innovation in treatment unless fever therapy for gonorrheal infections is excepted To say that every woman with a pelvic infection will be cured by the use of the vaginal heat treatments, regardless of all other factors, is obviously erroneous or to specify that a given number of treatments is the rule for a given type of infection will not in the final analysis be borne out.

Bacteria differ in their susceptibility to heat The gonococcus is much more heat labile than the streptococcus. However there are cases of gonorrheal infection in which the condition has resisted not only adequately administered vaginal heat treatments but an ordinarily sufficient number of well tolerated treatments in the fever cabinet. Heat alone, therefore, is not sufficient treatment in such cases.

The anatomical location of the infection influences response to vaginal heat treatment. A high-lying tubo-ovarian infection responds less readily than when such a condition is prolapsed in the cul-de-sac. Pelvic cellulitis or parametritis with extensive involvement of the perirectal tissues often responds slowly because heat administered through the vagina cannot be adequately applied It is possible also to employ a rectal applicator for the administration of heat to the pelvic viscera. This approach may be used for those patients who tolerate vaginal distention poorly or for those patients whose lesions are so situated that sufficient contact with the involved viscera cannot be secured through the vagina.

The resistance or state of the patient's immunity to the given infection of course plays an important part in the course of the disease. There are other factors also to be considered in the treatment in a given case of pelvic infection such as the age of the patient, extent of involvement of tissue, and the acuteness and chronicity of the condition.

It seems fair to state that vaginal heat treatments use in the treatment of pelvic infections of women, and that such treatment should be continued if improvement occurs. There are,

however, certain points regarding treatment by this method which merit discussion Some patients are intolerant to vaginal distention sufficient to afford an area for absorption of heat If the applicator is not distended, and if distention is not maintained throughout the treatment, no amount of heat will avail Pressure is therefore a vital factor in the proper dissemination of heat Pressure sufficient to distend the upper portion of the vagina and sufficient to apply the applicator to the cervix and vaginal fornices is an absolutely necessary condition to any degree of temperature, and if a patient will not tolerate this necessary pressure, one may as well discontinue this form of treatment When sufficient distention has been secured, the temperature employed is that which can be tolerated by the patient One is always suspicious of the patient who says that the treatment is entirely comfortable A check-up of conditions will usually reveal inadequate pressure It is a fair rule to look for slight discomfort during the course of treatment The pressure indicator on the machine is of some use in avoiding excessive pressure and definitely of use in noting changes in pressure indicating a faulty return of water The best guide to proper distention, however, is palpation either through the vagina or rectum This allows one to gauge accurately the sufficiency of distention

Too much emphasis may be placed on the temperature An ideal of 130 degrees F has been advanced The number of women who will tolerate this temperature with sufficient vaginal distention are few Investigation of a patient who is tolerating 130 degrees F without difficulty will often reveal a collapsed, or at best very incompletely distended, bag A temperature of 115 degrees F , for example, with adequate distention is more efficacious by far than attempting a higher temperature that must be given at lower pressure Women will vary greatly in their tolerance to heat and this tolerance must be determined for each patient Treatment based on these premises will lead to efficiency in the application of heat, and the results which may be expected of heat will usually be obtained

If the treatment is properly given, significant damage to the vaginal mucous membrane or cervix does not occur True, the vaginal wall is reddened after a treatment, blebs are common, and actual erosion may occur, and it is therefore well to make an inspection from time to time Skipping a treatment may occasionally be advisable In the period of active ovarian function, however, little damage is encountered For women beyond the menopause who have an atrophic vaginal mucous membrane and a contracted vagina, treatment by this method is to be very carefully observed and is, I believe, generally undesirable Fortunately, the necessity for treatment at this time of life rarely occurs

It seems fair to conclude on the basis of experience that heat may be conveniently, safely, economically, and efficiently applied to the vagina by this means The method has seemed to us satisfactorily to fill that rôle which heat may be expected to play in the treatment of pelvic inflammatory disease of women That this rôle may be played by other methods is without doubt true It is to be remembered that heat represents only one phase of treatment of pelvic infections

LAWRENCE M RANDALL.

MEMOIRS

WILLIAM HOLLAND WILMER
1863–1936

And when he fell, at sunset, he went down
As when a mighty cedar green with boughs,
Goes down with a great shout upon the hill
And leaves a lonesome place against the sky
——Edwin Markham.

THE sudden death on March 12 of Dr William Holland Wilmer leaves its "lonesome place" in the ranks of pioneers in the science of ophthalmology and surgery of the human eye. Of first importance in his profession,—as operating technician and teacher he kept his dynamic and winning personality to the sunset of his days and passed from this life laden with all the honor in the power of grateful patients and respecting colleagues to bestow

For many years I was associated with Dr Wilmer first as student, later as friend and colleague and I find it difficult to write of him with the calm and dispassionate pen of a true biographer His skill as an operator his aptitude for the speedy technique so necessary in many eye operations, in addition to his rare ability as an inspired clinician and his unusually keen flair for imparting his knowledge made those of us who studied under him feel fortunate indeed

Dr Wilmer's career ran true to the promise of his distinguished ancestry He was the son of the Right Rev Richard Hooker Wilmer and Margaret Brown Wilmer His father was the Protestant Episcopal Bishop of the diocese of Alabama. Their son, a native of Powhatan County Virginia born August 26, 1863 had the best of youthful educational opportunities, and he made the most of them. He received his medical degree from the University of Virginia in 1885.

He went immediately into an internship at Mt. Sinai Hospital in New York, where he served for 18 months, the first part of the time in general medicine, and later as resident in surgery He then became an assistant to Dr Emile Greening in private practice, and at the same time was able to teach at the New York Poly clinic Hospital Later he became connected with the clinic of Dr Agnew the ophthalmologist in New York It was during this period that he attended his own first private patients

In the fall of 1889 he actively entered the field to which he was to devote his life s energies and began the practice of ophthalmology in Washington D C.

Rapidly, through his manifold abilities, he achieved such distinction in his profession that honors were heaped upon him He found time from his busy practice to be professor of ophthalmology at Georgetown University and at the same time surgeon of the Episcopal Eye, Ear and Throat Hospital in Washington In 1919 Georgetown conferred on him the degree of LL D The last degree that Dr Wilmer was to receive was that same mark of honor, given by the Johns Hopkins University only a few weeks before his death

From his first days as a practitioner Dr Wilmer had had a splendid command of languages and had added to his first income by translating for some of the older surgeons As the years went by, he was able to travel in Europe and visit the famous clinics there, including Morfield, in England, and at the famous clinic in Vienna of the great Dr Adolph Fuchs, whose intimate friend he became

Dr Wilmer was, at the outbreak of the World War, a lieutenant in the Army Medical Reserve Corps He was immediately commissioned as major, and placed in charge of the Air Service Medical Research Laboratories at Mineola, Long Island As a director and inspiring force for those engaged in original research there he attained such recognition that in August, 1918, at the request of General Pershing, he was sent to France to become the chief of the Army's overseas medical laboratories He left the service with the rank of brigadier-general He was awarded the distinguished service medal on the citation of General Pershing Later, in 1924, he was made a commander of the French Legion d'Honneur

Following his war service, Dr Wilmer re-entered his private practice at Washington, which he renewed with an ever-growing success So many were his distinguished patients that when, in later years, he moved to Baltimore his examination chair was dubbed by the students the "Presidents' chair" Five of the chief executives of the United States had sat there as Dr Wilmer's patients

It was strange, to those of us who knew Dr Wilmer intimately, how occurred the growth of the public recognition of his greatness as an operator, diagnostician, and clinician, for he abhorred personal publicity and his professional life and works he attempted to keep a closed chapter, save as admiring associates might make them known

In fact, it was indicative of this aversion to personal promotion that he became violently opposed to the use of the telephone He insisted that telephoning was a waste of time All his appointments had to be made by letter, and he was meticulously on time His patients entered his office, one might say, on the stroke of a bell His busy office in Washington had a silent telephone and there was no listing in the directory At least from the time he came to Baltimore until his death, he rarely ever engaged in a telephone conversation

For lack of time Dr Wilmer was not able to gratify as fully as he would have liked his own urge for ophthalmological research Yet he recognized keenly the need of original inquiry in the field of the human eye, and ever bent his efforts

toward providing greater opportunities for others who came under his tutelage.

In 1922 his ability and sincere devotion to his patients crystallized into such an opportunity A group of those he had served joined together and raised a fund of $3,000 000 known as the William Holland Wilmer Ophthalmological Fund. This sum was used in the building of a model structure at the Johns Hopkins Hospital. It was named the Wilmer Institute and in 1925 Dr Wilmer was installed as its director also as professor of ophthalmology and ophthalmologist in-chief of the Johns Hopkins Hospital.

This Institution Dr Wilmer made a living monument to his work and ideals, as he saw to it that no effort was spared to provide within its walls every possible aid to research. The most scientific and delicate problems of the science of ophthalmology were given to the research workers who joined the staff of the Institute They labored under the direct guidance and inspiration of Dr Wilmer who spent long hours in the laboratories. From these laboratories have come many valuable contributions, responsible in no small measure for much of the advance made in ophthalmology during the past decade.

Significant of the humanity and generosity of the character of the man. Dr Wilmer insisted that at least three fourths of the beds at the Wilmer Institute should be for charity patients. He made his daily rounds of these wards and performed many of the complicated operations on those who were without funds On the occasion of such operations the entire staff of the Institute would attend as would many of the younger men from other departments of the hospital. Attendance at these events were experiences that stand vivid in the memories of us all

As the years swept on the Wilmer Institute grew in service to humanity and in importance to the profession with amazing rapidity Patients came from all over the world From many nations poured the requests for posts on the house staff

Although he had never been a prolific writer Dr Wilmer for years had dreamed of what was to be his monumental literary contribution to medical science —his *Atlas of the Eye* With the services of an unusual house artist at his command whom he had trained to use the ophthalmoscope and in possession of a wealth of most extraordinary material from his own clinical experience few members of his professional specialty were equipped as he was for such a task. He devoted many hours getting together the outline of what was to be this work and months and years of labor went into its actual production. In July of 1934 it was given to the profession,—a volume of impressive value containing 100 illustrations of fundi in full color each with the author's description and comment on the opposite page.

This work was not only an important contribution to ophthalmological knowledge, it was a practical working out of what had long been Dr Wilmer's

principle of teaching and practice He always had impressed on his students the value of picturizing what they saw within the eye and on the surface also, in making examinations and diagnoses He developed a set of rubber stamps which could serve as a sort of series of outline maps of the normal exterior and interior surfaces of the eye In making clinical records it was his teaching and practice to use these stamps, subsequently marking them so as to record infallibly the various abnormalities observed Thus Dr Wilmer's *Atlas* was another case of "hewing to the line" in following the precepts learned in his long and successful practice

The honors that have come to Dr Wilmer, both before and since his retirement from the Hopkins at the age of seventy, have been many Perhaps the climax of these was the occasion of the opening of the Institute This was conducted with much formality and ceremony, and many of Dr Wilmer's distinguished patients and the humbler ones as well held a reunion as the building was formally dedicated Perhaps, however, to Dr Wilmer there was no greater honor than that his friend of long standing, Dr Fuchs, made the long journey from Europe to address the throng assembled on the lawn before the Institute

In addition to the LL D degrees he received from Georgetown (of which he was a Regent) and from the Johns Hopkins, he was given the Sc D by Princeton He also found time for many associational activities, in most of which he took great interest, and in some of which he served as active leader

He was a member of the board of directors of the National Committee for the Prevention of Blindness and of the Advisory Committee for the Prevention of Hereditary Blindness He was a fellow of the American College of Surgeons and a member of the editorial staff of this Journal, its official organ, a member of the National Institute of Social Science, of the Committee on Mental Hygiene, honorary member of the Oxford Ophthalmological Society (England), Hungarian Ophthalmological Society, Chicago Ophthalmological Society, and the Saranac Medical Society He was a member of several patriotic organizations and veterans' groups

Dr Wilmer had served as president of the American Ophthalmological Society, of the Army and Navy Air Service Association, the Medical Alumni of the University of Virginia, Association of Military Surgeons of the United States and the Society of the Cincinnati of New Jersey

He was ever active in the church and took a considerable part in the upbuilding of the Protestant Episcopal Cathedral in Washington He was buried in the Chapel of St Joseph of Arimathea at the Cathedral One of the honors of which he was most proud was his award, in 1932, of the decoration of the Angelo Secchi Academy of Science at Georgetown University

His personal life was as full and felicitous as was his professional career In 1891 he was married to Re Lewis Smith of Pennsylvania She and their three

children, Richard Hooker and William Holland, Jr., and Mrs. Russell E. Sard survive him.

Dr Wilmer and Mrs. Wilmer were both passionately fond of gardening About equally distant from Washington and Baltimore—at Boyce Va., in the heart of the apple country—they found a lovely farm in a shady valley fronting a fine view of a nearby mountain ridge. There Dr Wilmer began his collection of evergreens which has been declared without a parallel in this country He grew and tended with care almost every variety cultivable in the Virginia latitude. Knowing of his work, the federal agricultural authorities leaned on his knowledge of evergreen trees and oftentimes it was he who first determined whether imported varieties were cultivable in the United States. When the *Atlas of the Eye* was finished, it was Dr Wilmer's intention, indeed, to write an authoritative work on evergreen culture. It is unfortunate that much of the priceless tree lore he acquired during the years passed away with him.

Indefatigable in his profession and with this avocation as a means of relaxing from the normal fatigue of his enormous activity Dr Wilmer went to his death without the usual curbings and circumscribings that we term *declining years*" In fact on Tuesday March 10 two days before he died, he had scheduled a list of operations for the day Friends in Washington had urged him to hold a meeting at his Washington home at which could be organized a branch Society for the Prevention of Blindness in the national capital.

Dr Wilmer postponed all his operations except one, Tuesday afternoon. He held the meeting, and the organization was formed. Two days later he was preparing to go to his office for his usual busy day when he was fatally stricken.

The death of Dr Wilmer is a severe loss to ophthalmology But to those of us who had the rare privilege of working with him, the loss is that of our truest friend.

Carey H. Bagley.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

IT would be difficult to find a group more qualified to write a treatise on the stomach and the duodenum than Eusterman and Balfour[1] Although thirteen other members of the Mayo Clinic have contributed chapters, the bulk of the work is by these two authors The chapter on the physiology of the stomach and duodenum, while written by an author well versed in this field, is too brief and incomplete and occupies too small a portion of the relatively large volume. It is the hope of the reviewer that in subsequent editions it may be considerably expanded Mann has given an excellent summary of his own very important experimental work on the pathogenesis of ulcer The pathology of the stomach and duodenum is ably discussed and the commoner lesions beautifully illustrated As might be expected, the bulk of the volume is devoted to the clinical picture, the diagnosis, and the treatment of gastric and duodenal ulcer and carcinoma The more infrequent lesions are, however, given thoroughly adequate consideration In the opinion of the reviewer, the book is by far the best in its field and the authors merit the thanks of both the physiologist and the clinician for their detailed and painstaking contribution It gives the reader access to the wealth of experience, observation, and medical and surgical judgment of a great clinic It will enjoy a wide circulation and perform a most useful service

LESTER R. DRAGSTEDT

THE title of Bailey's volume[2] well indicates its content A profusely, well illustrated book, it attempts to cover the vast field of objective surgical diagnosis in a manner heretofore seen only in larger volumes Rather than a complete text, it endeavors to cover its ground in outline form, a major criticism would be of the author's effort to condense a large subject into too small a text

The early portion of the work, dealing with elementary physical signs such as the head, neck, breast, tumors, ulcers, etc is excellently presented in detail There is some loss of balance in the latter part of the book in the handling of the major surgical conditions, particularly the acute and chronic abdomen, inasmuch as it gives the reader the sense of an important group of subjects intentionally shortened through an effort to complete the text in a limited space

The difference in approach between ours and English methods is occasionally manifest, but this is surprisingly well submerged It is perhaps most noticeable in the mention of certain physical signs and methods that are not emphasized in our teachings, but such is only in the point of emphasis and not in regard to interpretation

The author has reduced his subject exceptionally well to a concise, pointedly illustrated compens form, and as such it should prove an attractive reference book for the student and practitioner

MARSHALL DAVISON

THAT Karsner's *Human Pathology*[3] appears in a new edition—the fourth in 10 years—is sufficient evidence of its merits Revision of a textbook of pathology involves more than the mere addition of new material A comparison of this edition with earlier ones reveals many changes in arrangement and in the amount of space allotted to different subjects On the whole, these changes have been improvements Much new material has been incorporated in this edition, especially in the chapters on glands of internal secretion and on tumors The latter chapter has been almost entirely rewritten The amount of new material added is indicated by the inclusion of over three hundred new references in the bibliography The bibliography is worthy of special mention It is more extensive than that in any other American textbook of pathology For example, the bibliography on "Tumors" contains 192 titles, on the "Alimentary Canal," 209 and on the "Ductless Glands," 217 The usefulness of the bibliography is greatly increased by the inclusion of the complete title of each reference

Although this is essentially a textbook of gross and microscopic pathology, the author does not neglect the functional disturbances which result from the structural changes induced by disease Such a book is a dependable, needed, and safe guide at a time when so much emphasis is being placed upon pathological chemistry and physiology to the neglect of the more fundamental structural changes Gross and microscopic pathology are still the solid base upon which any science of disease must rest if it is to have a secure foundation. The present volume presents pathology as such a foundation together

[1] THE STOMACH AND DUODENUM By George B Eusterman M D F.A.C.P, and Donald C Balfour, M B, M.D (Tor), LL.D F.A C.S F.R.A.C., and Members of the Staff of The Mayo Clinic Philadelphia and London W B Saunders Co, 1935

[2] DEMONSTRATIONS OF PHYSICAL SIGNS IN CLINICAL SURGERY, By Hamilton Bailey, F.R C.S (Eng) 5th ed rev Baltimore William Wood & Co. 1935

[3] HUMAN PATHOLOGY; A TEXTBOOK. By Howard T Karsner, M.D With an introduction by Simon Flexner M.D 4th rev ed Philadelphia and London J B Lippincott Co, 1935

with parts of the superstructure of disturbed chemistry and function, thoroughly integrated and later related, as they should always be with their basic structural causes. The author has shown an adequate sense of proportion and of the relative importance of the different phases of pathology, and has thus produced a well balanced book which can be heartily commended to internists, surgeons, and medical students.

J. P. Simonin

MANY years of experience in teaching students has qualified the authors especially well to write this latest book on otolaryngology. Bearing in mind the problems confronting a student of otolaryngology Imperatori and Burman have endeavored to present their subject in outline and readable form, placing special emphasis on and describing in detail the more frequently encountered conditions, and mentioning only briefly the less common disorders.

The recent broadening of the field of otolaryngology has made it necessary to include chapters on physical therapy and radiation. These chapters are of necessity incomplete but they serve to remind the student of such therapeutic aids. The chapter on allergy is relatively brief for such a comprehensive subject, and the chapter on laboratory aids could well be left to a special text. A welcome addition is the chapter on diseases of the floor of the mouth and salivary glands.

The book is a one volume work of 900 pages and 480 illustrations, and is essentially the course given to students in the graduate department of Columbia University. The format of the text is such as to make it easy to read, and the undergraduate should find in it a useful outline to follow in studying diseases of the nose and throat.

Jonas Dozier

THE book by the Crossens entitled *Diseases of Women*[1] was written for the use of students, and is limited chiefly to medical gynecology rather than operative gynecology as are most textbooks.

In general, the book seems to answer the need of the student fairly well. It covers the subject and we think that the student would make no mistake in using it as a guide. Some of the chapters are particularly good, such as the one on extra-uterine pregnancy. The illustrations are generally clear and well chosen, although some of them are not reproduced as well as they were in their original texts. The photomicrographs are excellent. There are certain particulars, however, in which we think the book could be definitely improved. The fault lies in some instances probably, in the arrangement of the subject matter rather than in oversight.

A complete picture of a disease entity is not always given for in this book the discussion of each anatomical unit are considered separately. Therefore, to get a clear picture of gonorrhea, tuberculosis, puerperal infections or childbirth injuries, as examples, the student must read disjointed paragraphs in many sections of the book. Because of this, perhaps, the symptomatology of some of these conditions is disconnected and the clinical course of the disease is not presented as a unit. This lack of unity makes the book hard to read. It is more like an encyclopedia than a summary of experience.

The arrangement of the book perhaps accounts, too, for the fact that subjects are not always presented from the historical viewpoint, when they are reference is made usually only to the work of men still living. The student therefore learns little of how the information was assembled or who were the founders of modern gynecology. The book contains no bibliography and we consider this a decided loss to those who would like further information.

The book is too big, 999 pages. We wonder whether the particular type of arrangement has not contributed definitely to its bulkiness. For example, the authors have tried to condense pathology into one chapter but under each subject have been compelled to repeat the pathology at times in great detail. Similarly reference must continually be made to other parts if the subject matter is not repeated. It is possible also that the large amount of space given to endocrinology throughout the book might be condensed. It is also questionable whether a text on medical gynecology should include a chapter on the instruments needed to perform a major gynecological operation.

The chapter on congenital anomalies does not refer to the development of the genito-urinary apparatus as a unit or to the consequent frequency with which urinary anomalies are associated with defects in the reproductive organs. In the discussion of methods of treatment of various diseases, end-results are not often mentioned. Symptomatology is often abbreviated. However when the authors discuss a subject as a unit, the results are admirable, as for example in the chapters on myoma of the uterus, on cancer and on extra-uterine pregnancy.

The usefulness of this book cannot be questioned. One likes to learn the views of others, even when he does not always agree. The book would be particularly helpful to students whose teachers divide the subject matter as it is done in *Diseases of Women*. The ideal book, perhaps, would attempt to present the subject matter from both viewpoints, so that the student might gain a concise idea not only of the pathological processes that affect a given organ, but also of disease entities as a whole.

The book presents an interesting combination of the new and the old, its stress on endometrin and ergot and the use of rubber tube drainage in pelvic abscess carries one back to the days of Lapoyrouse, while the enthusiastic discussion of experimental endocrines is a vital question of today.

LAWRENCE R. WEAVER.

[1] DISEASES OF WOMEN. By Charles J. Imperatori, M.D., F.A.C.S., and Herman J. Burman, M.D. Philadelphia, London and Montreal: J. B. Lippincott Co., 1941.

[1] DISEASES OF WOMEN. By Harry Sampson Crossen, M.D., F.A.C.S., and Robert James Crossen, M.D., 4th ed. St. Louis: The C. V. Mosby Co., 1941.

IN his book *Mechanics of Normal and Pathological Locomotion in Man*[1] Steindler presents the subject from a physical point of view The material is taken from lectures to students in orthopedic surgery and physical education

Mathematical sciences are important in physical education and in surgery of the locomotor system The author intends to translate theoretical conceptions of physical science into terms of practical application The book presupposes a knowledge of elementary physics and mathematics, fortunately, it contains a preamble of mathematical laws and physical conceptions that apply to the subject of human locomotion The author realizes the gargantuan size of his undertaking, and that there are pertinent facts in human locomotion to which mechanical analysis can not be applied

The history of the mechanics of locomotion is reviewed from Haller to the present day The center of gravity is studied and its altered position in the development of the human race Stresses and the theory of columns are applied to bony structure The powers and properties of normal muscle are considered as well as pathological muscles and their altered effect in action The chapter on fatigue and recovery is informative and of interest to every practitioner

The book is divided into two parts, the second part being concerned with special mechanics of locomotion In a study of the spine the structures and the active forces are discussed from a mechanical point of view The interpretation of anatomical and physiological changes in the spine in the terms of mechanics is of practical significance in the problem of poor posture and scoliosis Each individual joint is studied as a mechanical problem There is a thorough description of normal walking The normal movements involved in running and in the more common competitive sports are analyzed The pathological gait is clearly portrayed by means of ingenious sketches Rationalization of the mechanics of locomotion is described as an attempt to determine the optimal efficiency of the body as a machine

The author succeeds in gathering the present knowledge of the mechanics of human locomotion in this one volume The subject material, the use of formulas and diagrams, and the characteristic style of the author require thoughtful reading The book will serve as a source of information to any one interested in the problems of locomotion

EMIL D W HAUSER

IN his new 166 page book *Tumors of the Urinary Bladder*[2] the author, Edwin Beer, has completely covered the subject of bladder neoplasms The text has been written so as to present the subject in a concise, interesting and readable manner

The various chapters include history, classification, pathology, symptoms, diagnosis, and treatment The author has presented a simplified classification which is applicable to clinical and pathological criteria The major portion of the book has been devoted to therapy The technique and results of the various therapeutic methods have been well described and the more complicated procedures illustrated

The statistical data, which tabulates the type of treatment and results, has been acquired from 600 cases treated by the author and his associated staff

This book should be helpful to the physician or student who desires concise and accurate information concerning tumors of the urinary bladder

HARRY CULVER.

IN collecting, arranging, and annotating the material of *Classical Contributions to Obstetrics and Gynecology*,[3] Herbert Thoms has rendered a distinguished service, particularly to those interested in these branches of medicine

This small volume is a moving legend of the men and women whose efforts have resulted in the preservation of life to countless mothers and babies In it we trace the halting steps by which the modern obstetrician and gynecologist has achieved his present competence It is a fine refutation of the often heard remark ' writing papers is a futile business " It must be true that the observations recorded in the 59 papers reviewed had been noted by many of equal wisdom, but they were of no value to the world until they were written down

There are abstracts from the writings of Hippocrates, but they are brief The book really begins with a description of the uterus by Soranus of Ephesus (second century A D) and covers most of the important contributions from his time to the beginning of the present century Each abstract is preceded by a brief but comprehensive biographical sketch of the author The illustrations are adequate None of the abstracts is without interest A list of the major contributions or even those of most importance is impossible, but there are some which stand out as beacons that have lighted the progress of all medicine There is Hendrich Van Deventer's classic description of the bony pelvis, and the first record of the fetal heart by Lejumein The first use of analgesia by Sir James Young Simpson, the use of obstetrical forceps by William Gifford, and the suggestion of primary perineorrhaphy by Mauriceau are given in detail The chapter on puerperal sepsis is complete and divides the credit for its prevention more fairly than is usually done The magnificent directions which Smellie gave for the proper application of forceps are still hard to better

The description of the first ovariotomy by Ephraim McDowell Sims' article on the treatment of vesico vaginal fistula, Tait's contributions on

[1] MECHANICS OF NORMAL AND PATHOLOGICAL LOCOMOTION IN MAN By Arthur Steindler, M D F A C S Springfield Ill and Baltimore Md Charles C Thomas 1935

[2] TUMORS OF THE URINARY BLADDER By Edwin Beer M D Baltimore The Williams and Wilkins Co 1935

[3] CLASSICAL CONTRIBUTIONS TO OBSTETRICS AND GYNECOLOGY By Herbert Thoms M D With a foreword by Howard A Kelly Springfield Ill and Baltimore Md Charles C Thomas, 1935

ectopic pregnancy and Emmet's treatment of cervical lacerations are not only high spots in this book, but are the historic background for modern surgery.

If there is any criticism to be made of Dr. Thoens' volume it may be said that it would be more satisfactory to the average reader if it were arranged on a wholly chronological basis instead of being divided according to subject matter. One leaves this book with a wish that there could have been more of it.

J. E. Fitzgerald

IN HIS book[1] discussing rarefying conditions of bone, which may be caused by osteoporosis, decalcification or replacement by other tissues, King groups together by their common essential feature, a disappearance of calcium salts. The clinical groups mentioned in the title of this book are based on the roentgenological appearance, or translucency study of bone. With the premise that in osteoporosis both osseomucin and calcium salts are resorbed, whereas in decalcification the lime salts alone are removed, this author states that the essential limitation of roentgenological interpretation is that a number of different microscopical structures may give rise to the same X-ray appearance and an accurate diagnosis can be made only from the special associations of diminished and increased density together with the clinical history. But there is great limitation of information when only a small particular part of the film or skeleton is viewed and it is not usually possible to say which tissue is causing the abnormality. This limitation must be recognized since different pathological conditions may give similar roentgenological findings. One must realize that one is dealing with a roentgenological syndrome and not necessarily with a specific disease.

An attempt is made to show that an appreciation of the possible sources of error which occur in the localized rarefying diseases of bone, may solve many of the difficulties of classification of these diseases.

In the second section, the effects of osteochondritis on different bones, from tarsus to spine, also types of post-traumatic rarefactions of bone, are described. For the student, the most valuable feature of the work is to find these various disparate changes of bone discussed between two covers. The brevity of the text on some of the subjects is startling, but there are satisfying bibliographies at the end of each chapter. This volume makes a valuable addition to the library of any student of osseous pathology.

Kellogg Speed

[1] Localized Rarefying Conditions of Bone, as Exemplified by Lime-Poverty, Disease, Osseo-Sclerotic's Disease, Kienböck's Disease and Related Conditions. By A. J. J. King, M.D., D.Sc., M.B. (Melb.), F.R.C.S. (Eng.), F.R.A.C.S. Baltimore: Williams & Wilkins Co., 1931.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

Oxford Medical Publications. *The Natural History of Disease.* By John A. Ryle, M.A., M.D., F.R.C.P. London: Oxford University Press, 1936.

The Specificity of Serological Reactions. By Karl Landsteiner, M.D. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1936.

Psychology of Sex: A Manual for Students. By Havelock Ellis. New York: Emerson Books, Inc., 1935.

Transactions of the American Gynecological Society. Volume 60 for the year 1935. Edited by Otto H. Schwarz, M.D. St. Louis: The C. V. Mosby Co., 1936.

The Single, the Married and the Married. By Maurice Chideckel, M.D. New York: Emerson Publishing Co., Inc., 1936.

Basal Metabolism in Health and Disease. By Eugene F. DuBois, M.D. 3d rev. ed. Philadelphia: Lea & Febiger, 1936.

Oxford Medical Publications. *Detachment of the Retina: Operative Technique in Treatment.* By J. Cole Marshall, M.D., F.R.C.S. London: Oxford University Press, 1936.

Oxford Medical Publications. *The Early Diagnosis of Malignant Disease, for the Use of General Practitioners.* By Malcolm Donaldson, F.R.C.S. (Eng.), M.B., B.Ch. (Cantab.), F.C.O.G., Stanford Cade, F.R.C.S. (Eng.), William Douglas Harmer, M.A. (Camb.), M.C. (Camb.), F.R.C.S. (Eng.), R. Ogier Ward, M.Ch. (Oxon.), F.R.C.S. (Eng.), Arthur Tudor Edwards, M.A. (Camb.), M.D., M.Ch. (Camb.), F.R.C.S. (Eng.). London: Oxford University Press, 1936.

Medical History of Contraception. By Norman E. Himes, Ph.D. Medical Foreword by Robert Latou Dickinson, M.D., F.A.C.S. Baltimore: The Williams & Wilkins Co., 1936.

California Medical Association. *Cancer Commission Committee Studies.* San Francisco, Cal.: J. W. Stacey, Inc., 1936.

Der Leib in Seiner Entwicklung: Sein Hirnkorper und seine Wirkung in Anwirkung. By Prof. Dr. Erich Schneider and Dr. Phil. Ernst Wilhelmi. Stuttgart: Ferdinand Enke, 1936.

SURGERY, GYNECOLOGY AND OBSTETRICS

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AN EXPERIMENTAL STUDY[1] OF URETERO-INTESTINAL IMPLANTATION

I THE CAUSE OF PERITONITIS

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ASSISTED BY

WILLIAM K MURPHY, M D, T BRENT WAYMAN, M D, H J McCORKLE, M D, AND F H BENTEEN, M D, SAN FRANCISCO, CALIFORNIA

NO method of uretero-intestinal implantation in general use has proved its outstanding superiority Probably the manner of execution (technique) is as much at fault as the method which is used Poor workmanship in the performance of the operation can be responsible for as many failures as the flaws in the method itself The brilliant successes which have been obtained occasionally by almost any of the many different methods which have been used, lead to the conviction that uretero-intestinal implantation is feasible and that a method which is superior is possible, in other words, that a plan of operation will become sufficiently standardized, even when put to general use, to minimize failures The method must be planned not only to prevent the complications which cause failure but also to permit good performance by different surgeons This demands simplicity of technique

The immediate risks of ureteral implantation, aside from shock, pneumonia, etc, are

1 Infection (a) peritonitis, both local and general, (b) infection of the abdominal wound, (c) infection about the ureter where it enters the bowel, which may lead to peritonitis or ureteritis, (d) ureteritis and pyelonephritis (both ascending and hematogenous)

2 Ureteral obstruction which has a variety of causes, such as (a) surgical edema, (b) constriction and kinks caused by the method and manner of anastomosis, (c) bands and adhesions, (d) inflammation, periureteral, interureteral, and intra-ureteral, (e) anemic necrosis, (f) neurogenic stasis ureteral atony, and dilatation

Many of these complications are more imminent with some methods than others For this reason perhaps the incidence of peritonitis varies in the different statistical reports For example, Ssolowoff gave peritonitis as the cause of death in 10 of the 14 deaths in his series of 30 cases, and Coffey, in 4 of the 9 deaths in 35 cases (Table I) Cabot reported 14 consecutive uretero-intestinal implantations for exstrophy of the bladder without an operative death However, 21 of Ssolowoff's patients had vesical carcinoma and only 1 had exstrophy Seventeen of Coffey's patients had cancer and 10 had exstrophy Furthermore in Mayo's experience, transplantation of each ureter separately, for exstrophy in children, is safer than simultaneous bilateral implantation It is necessary, therefore, to analyze different reports not only with respect to the factors of method and technique as affecting the results, but also with regard to the ages

[1]Supported by the Christine Breon Fund for Medical Research.

and the conditions of the patients Two of the 4 deaths from peritonitis reported by Coffey were in children with exstrophy One of my patients with carcinoma of the bladder died of peritonitis following cystectomy 6 weeks after the ureteral implantation. This death bore no relation to the implantation It may be stated however that irrespective of the method used of the condition for which it is used, or of the age of the patient, peritonitis appears frequently in the statistical reports on uretero-intestinal implantation as being the cause of failure

It is reasonable to assume that the peritonitis in these cases was caused by leakage at the site of the implantation after the operation had been completed and not by contamination at the time of operation. It is very important that these two sources of infection be distinguished When this is done opening the bowel does not appear so prohibitive, and the elaborate methods recently designed by Higgins (1932) and by Poth (1935) to prevent contamination at the time of transplantation are not so essential

A great deal of work on intestinal resection and anastomosis has shown that the peritoneal cavity can care for considerable contemporary contamination However the least bit of leakage because of imperfect suturing or sutures tearing out after closure invariably is fatal Almost 50 years ago (1887) Halsted completed an experimental study of intestinal suture This contribution developed certain facts which remain today as the fundamentals in intestinal surgery and can be read with profit by every urologist doing uretero-intestinal implantations He wrote "We are brought therefore to the conclusion that the chief danger of infection of the peritoneum is from the passage of the intestinal contents (bacteria) into the peritoneal cavity subsequent to the operation The conditions which may lead to this unfortunate occurrence are (1) failure to close completely and firmly the wound of the intestine (2) penetration of the intestinal lumen by one or more sutures (3) giving way of the sutures (4) ulceration or sloughing of the intestine at the site of suture These four conditions which cause peritonitis subsequent to intestinal resection occur likewise following implantation of the ureter Halsted's next statement "In order to bring about complete and firm closure of the abnormal opening into the intestine, it has been customary to make several series of sutures of the intestine one over the other in the form of the so called *Etagennaht* In this way a considerable extent of the intestinal wall is folded in the circulation of which is greatly impeded There are especial dangers which attend the folding in of an unnecessarily large amount of intestinal wall for on the one hand, this increases the extent of tissue which undergoes sloughing and thus increases the danger of infection, and on the other hand, the flange formed by the folds projecting into the intestinal lumen is an obstacle to the passage downward of the fæces, which, accumulating at and above the site of suture, increase the tension upon the sutures and endanger their separation Applying these principles to the problem of ureteral implantation it is evident that in addition to the risks of sloughing and giving way of the sutures, a method of closure in layers by rows of sutures increases the likelihood of ureteral constriction The need of a simple method of closure is obvious Furthermore, the added suturing of the intestinal wall required by closure in layers increases the chance of one or more of these sutures accidentally penetrating the intestinal lumen Finally to quote Halsted further "Any one by a simple experiment, can convince himself how frail is the hold of sutures which include only serosa and muscularis I am inclined to regard perforation of the gut wall on the one hand and tearing out of stitches on the other as the leading factors in the production of the peritonitis which has brought about the fatal issue in many cases of intestinal suture"

The causative factors producing peritonitis, such as method on the one hand and technique on the other may be studied experimentally and the following pages present such a study

EXPERIMENTAL STUDY OF THE CAUSE OF PERITONITIS

Ureteral implantation, simultaneously bilateral except in two instances (serial Nos 26 and 50, Table II) was performed on 53 dogs

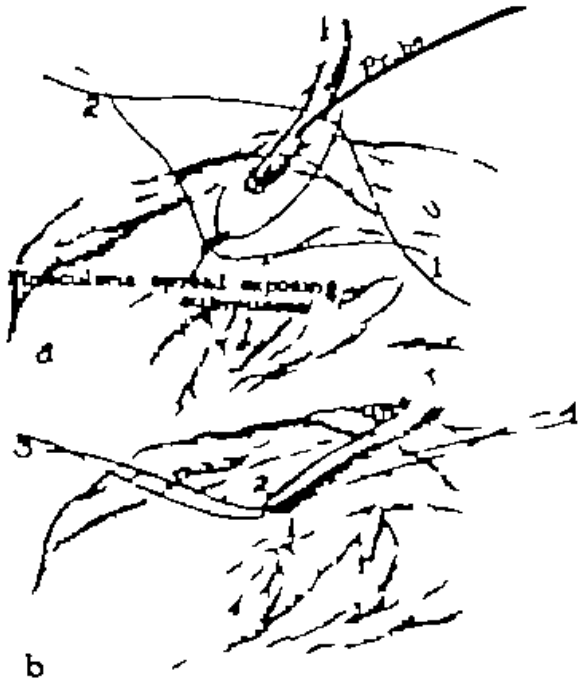
TABLE I

Condition	Surgeon	Number of patients	After implantation		After cystectomy		Total		
			Living	Dead	Living	Dead	Living	Dead	Died of peritonitis
Urethral occlusion	Ssolowoff	3	1	2					
Ureterovaginal fistula	Ssolowoff	1	1						
Hunner ulcer	Personal	1		1					
Vesicovaginal fistula	Ssolowoff	3	1	2					
	Coffey	4	3	1					
	Personal	4	2	2					
Tuberculous ulcers of the bladder	Ssolowoff	1	1						
	Coffey	4	3	1					
	Personal	7	7						
Hypertrophy of the bladder	Ssolowoff	1		1					
	Coffey	10		3	6	1			
	Personal	11		1	7	3			
Carcinoma of the bladder	Ssolowoff	21	4	7	8	2			
	Coffey	17		8	6	3			
	Personal	17	3	3	5	6			
Summary	Ssolowoff	30	8	12	8	2	16	14	10
	Coffey	35	6	13	1	4	18	17	4
	Personal	40	1	7	12	9	4	16	
Total		105	6	5	32	15	58	47	16

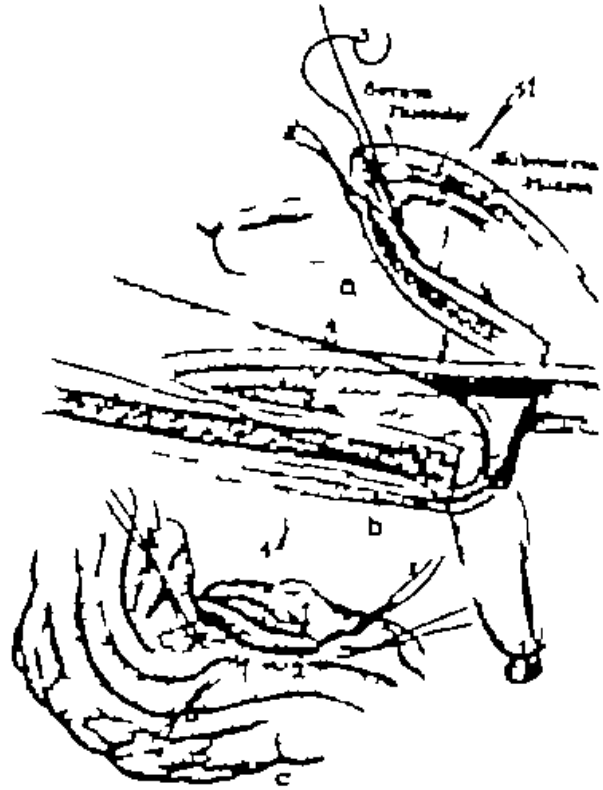
by 10 different methods (Table II) The bowel was opened at the time of the operation in all but the 5 dogs on which Higgins' method was used In 40 dogs (serial Nos 9 to 48 inclusive, Table II) variation of technique was slight and is indicated sufficiently by the accompanying drawings Thirteen of the 53 dogs died of peritonitis The experiments were not planned solely for the study of peritonitis The poor results obtained were fully anticipated in most cases The significance of suturing and overlapping of the bowel to necrosis and leakage fully demonstrated by Halsted and others needs no confirmatory study The results however indicate, as anyone might predict that the risk of peritonitis is much greater by some methods than by others

1 *Experimental evidence of contamination at the time of operation as a cause of peritonitis* Experimental and clinical experience in intestinal suturing minimizes the risk of peritonitis from contamination with intestinal contents at the time of operation This conclusion was tested personally on dogs a number of times The bowel was incised and opened as for ureteral implantation Instead a probe was inserted and well soiled, then withdrawn and the dirty end smeared about over the bowel and neighboring loops The incision in the bowel then was closed None of these dogs showed any evidence of local or general peritonitis

In the course of opening the bowel 96 times in the 48 dogs for the implantation of ureters gross contamination occurred at this time in 6, by the leaking out of the contents of the bowel in 2 and by the ureter's slipping out, or having to be withdrawn after insertion and reinserted in 4 Considerable soiling of the operative field was obvious in these 6 cases and it probably occurred to a lesser degree in others In none was this type of contamination responsible for peritonitis Nevertheless this source of contamination is a potential risk and the plan of any operation should be to reduce it to a minimum by proper preoperative preparation of the bowel and by the



Fig



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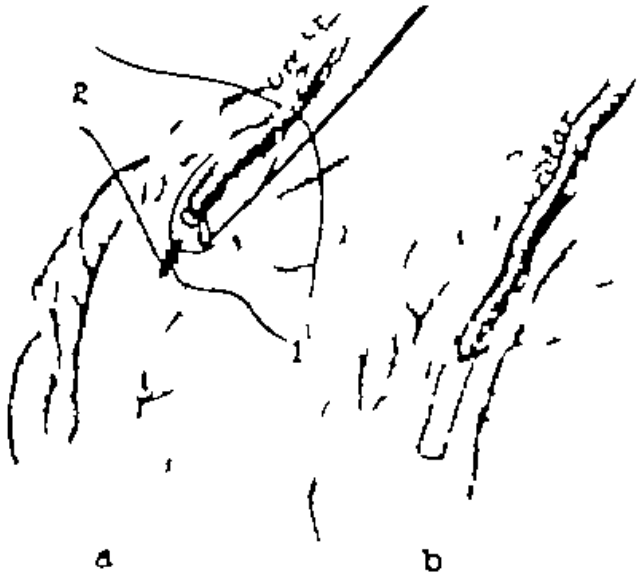

Fig 3

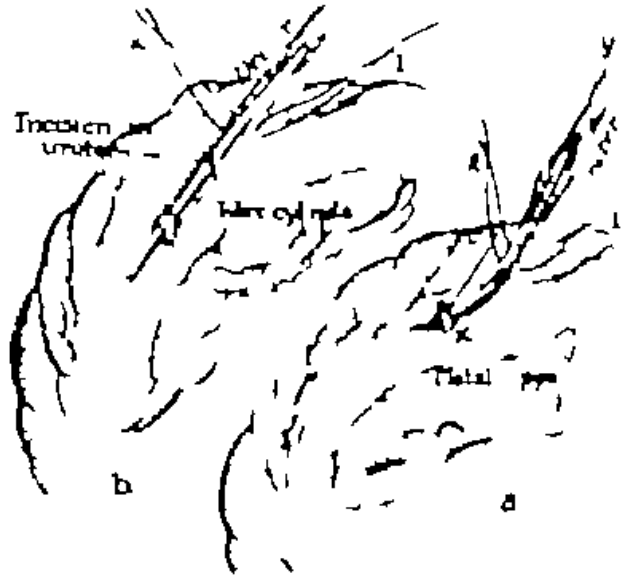

Fig 4

Fig Direct insertion of the ureter which is anchored with two sutures, 1 and The short incision is closed with one suture on each end, 3 and 4 a, The anchoring sutures placed in the submucosa of the intestine and the adventitia of the ureter b, The end of the ureter has been pushed through small stab incision of the submucosa and mucosa layers. Sutures 1 and ha been tied Sutures 3 and 4 close the muscularis about the ureter

Fig Diagrammatic representation of the manner in which the ureter is anchored in the all of the intestine by the simple seven suture method a, The sutures and 1 anchor the ureter snugly in the small opening through the submucosa and mucosa made by the cautery Note that this slit should not be too large but of a size as indicated by the dotted circle equal to the diameter of the ureter b The unconstricted anastomosis c, Sutures 4 and 5 anchor the ureter to the trough of the incision Sutures 6 and 7 (shown in b) bring together the serosa and muscular layers over the point of penetration without constricting the ureter

Fig 3 Same as Figure except that the end of the ureter is not slit The end ligature is left with loop which is caught by groove on the end of probe After insertion

Applications of this method in cases published in detail in Surgery Gynecology and Obstetrics.

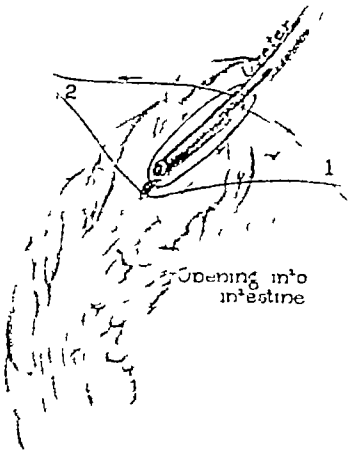

Fig 5

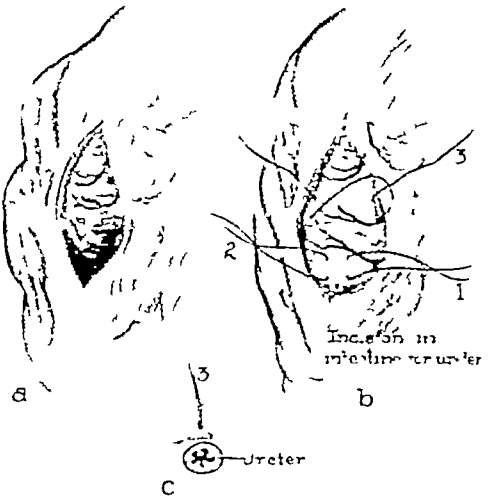

Fig 6

Fig 7

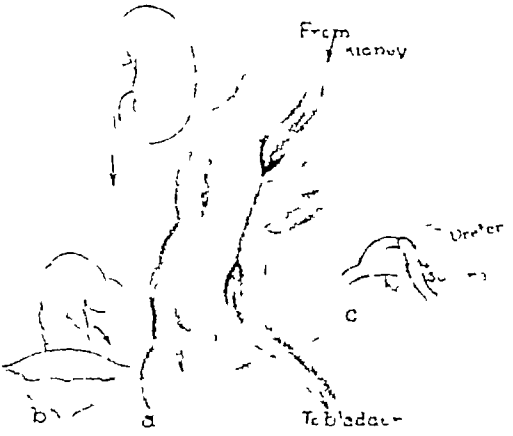

Fig 8

of the ligature the loop can be pushed off by the probe, leaving the ureter open at the end

Fig 4 Cylinder method of insertion of the ureter without the use of a probe. a, A metal spear is tied in with a bow knot at *x* so that, after insertion, the knot can be untied by pulling the long arm *x*, and the spear pushed out of the ureter into the bowel b, A wax cylinder impregnated with merthiolate

Fig 5 The use of a segment of a catheter as a cylinder

Fig 6 Implantation with a submucous fold a Large surface of submucosa exposed b, Sutures *1* and *2* placed in the submucosa at the lower end and through the adventitia of the ureter (not shown) as in Figure 2 Suture *3* is a mattress so placed that when tied it brings the submucous layer around the ureter completely as shown in c c The submucous fold about the ureter

Fig 7 A flap of muscularis is made to cover the ureter after insertion

Fig 8 Illustrates the method of Coffey Higgins a The undivided and intact ureter as shown in b) has been imbedded to the submucous layer c The hidden suture which cuts through later to form the orifice into the bowel

use of the best asepsis which is possible with the method used

B Experimental evidence of leakage after operation as a cause of peritonitis Leakage of the contents of the bowel into the peritoneal cavity was demonstrated by distending the bowel at the time of the postmortem examination in 9 of the 13 dogs which died of peritoni-

TABLE II

Method	Serial No.	Group No.	Protocol No.	Date of operation	Date of death	Duration	Cause of death	Remarks
Direct ureteral method (Fig.)			34	[illegible]	[illegible]	4 days	Infection of abdominal wound. Peritonitis	No urine leakage, abscess at site of right implant
			298	[illegible]	[illegible]	3 days	Infection of abdominal wound. Peritonitis	Leakage
		3	37	[illegible]	[illegible]	3 days	Infection of abdominal wound. Peritonitis	Leakage
		4	3	[illegible]	[illegible]	day	Infection of abdominal wound. Peritonitis	Leakage
Partial intravesical method (ureters and ureteral end crushed)	5		37	[illegible]	[illegible]	5 days	Infection of wound. Peritonitis	Leakage (urine) from stump of ureter at site of implantation
	6		33	[illegible]	[illegible]	days	Infection of abdominal wound. Acute pyelonephritis	
	7	3	[illegible]	[illegible]	[illegible]	3 day	Ureteral reflux from stump. Acute pyelonephritis	Ureteral end crushed in anastomosis at site of implantation
	8		[illegible]	[illegible]	[illegible]	4 mos.	In good condition. Killed	Bilateral pyelonephrosis
Intravesical (ureters method) A. Probe and scissors (Fig.)	9		[illegible]	[illegible]	[illegible]	7 mos.	Killed	Hydronephrosis on left
	10		[illegible]	[illegible]	[illegible]	7 days	Peritonitis	Right ureter pulled loose
		3	48	[illegible]	[illegible]	6 mos.	Killed	Slight bilateral hydronephrosis. Ureteral kink on right
			77	[illegible]	[illegible]	6 mos.	Killed	Good result
	2	5	84	[illegible]	[illegible]	days	Evisceration	Infection at site of transplant. No leakage
	3	6	86	[illegible]	[illegible]	14 days	Uremia	Ureteral kink on right, stenosis on left
B. Grasp of probe (Fig. 3)	3	7	[illegible]	[illegible]	[illegible]	mos.	Convulsions, coma, unknown	Blood urea, [illegible] on day of death. Vacuolated hydro ureter
	5	8	486	[illegible]	[illegible]	4 days	Evisceration	No leakage. Good transplant
	17	9*	3	34	1	3 day	Retroperitoneal abscess. Peritonitis	Leakage at site of left implant
	8	10	33	[illegible]	[illegible]	mos.	Infection of abdominal wound. Bilateral pyelonephrosis	Ureteral pulled. No leakage
C. Metal spoon open (Fig. 4, a)	9		35	[illegible]	[illegible]	day	Left pyelonephrosis	Left pulled. Right side good
	10		[illegible]	[illegible]	( ) Right [illegible] ( ) Left [illegible]	3 mos.	Killed [illegible], overstretched	Right hydronephrosis
D. Wax cylinders (Fig. 4, b)		3	34	[illegible]	[illegible]	mos.	Infection of wound. Pyelonephritis	Reflux at left. No leakage
			36	[illegible]	[illegible]	mos.	Killed	Good result
	3	3	33	[illegible]	[illegible]	3 days	Peritonitis	Ureteral perforation and transplants in good condition
	14	10	[illegible]	[illegible]	35	mos.	Condition good. Killed	Slight dilatation on both sides
E. Tube catheter (Fig. 5)	15	7	[illegible]	[illegible]	[illegible]	3 days	Acute suppurative pyelonephritis (left). Infection of wound	Right kidney appears normal
	16	18	345	[illegible]	[illegible]	day	Acute suppurative pyelonephritis, bilateral	No per urinam
	17	4	[illegible]	[illegible]	[illegible]	[illegible] mos.	Killed	Good transplants
F. Probe and scissors	18	10	97	[illegible]	[illegible]	day	Abscess of lung	Slight hydronephrosis. Good transplants
	19			34			Peritonitis	Left ureter had slipped out
	20		97	[illegible]	34	mos.	Killed	Good transplants
		3	[illegible]	[illegible]	[illegible]	days	Infection of wound. Peritonitis	Left renal implant. Right is good
			33	[illegible]	[illegible]	days	Uremia	Ureteral obstruction from ureter into adhesions

Dead of peritonitis

TABLE II —Continued

Method	Serial No	Group No	Protocol No	Date of operation	Date of death	Duration	Cause of death	Remarks
Probe and cautery	33	25	144	8-17-34	9-18-34	1 mo	Killed	Good transplant
	34	26	236	1- 4-35	2- 4-35	1 mo	Killed	Hydronephrosis
	35	27*	269	3- 8-35	3-13-35	5 days	Left ureter perforated with suture No 1 Peritonitis	Urinary leakage
	36	28	279	3-14-35	5- 4-35	1 mo and 20 days	Pyonephrosis	At time of operation the right ureter was perforated by suture No 1 and then ligated purposely
	37	29	275	3-14-35	3-20-35	6 days	Cause undetermined	Good transplant
	38	30	321	4- 4-35	6-21-35	2 mos	Bilateral pyonephrosis	
	39	31	338	4-11-35	8- 2-35	4 mos	Left pyonephrosis Slight hydronephrosis on right	
	40	32	3 7	4-18-35	4-21-35	3 days	Sepsis from infection of abdominal wound	Infection at site of implant No peritonitis
	41	33*	342	4-25-35	4-30-35	5 days	Male, voided during operation, contaminating the wound Peritonitis	Leakage on left
Submucosal Fold method (Fig 6)	42	1	239	1- 4-35	4- 2-35	3 mos	Killed	Marked left hydronephrosis slight on right
	43	2	489	1- 8-35	1-15-35	7 days	Infection of wound Uremia	No peritonitis Hydronephrosis
	44	3	246	1- 8-35	2- 9-35	1 mo	Right pyonephrosis Infection of wound	No peritonitis
	45	4	263	1-16-35	1-21-35	5 days	Infection at site of implant. Acute pyelonephritis Infection of wound	No leakage
	46	5	242	1-16-35	2- 9-35	24 days	Right, pyonephrosis Left good Moderate infection of abdominal wound	No peritonitis
Muscularis Flap method (Fig 7)	47	1	309	2- 1-34	2- 5-34	4 days	Evisceration	
	48	2*	105	7-31-34	8- 3-34	4 days	Infection of abdominal wound Peritonitis Right ureter sloughed out	
Higgins-Coffey method (Fig 8)	49	1	265	(1) 1-31-35 (2) 2-13-35	2-26-35	13 days	Acute pyelonephritis (bilateral) Pneumonia	At the second operation there was found to be no drainage into the bowel on the right This ureter was re-implanted by the 7 suture method
	50	2†	43	(Right only) 2-30-34	9-18-34	7 mos	Killed	Well marked hydronephrosis
	51	3*	268	1-31-35 2nd stage not done	2-28-35	8 days	Infection of wound with abscess perforating into abdominal cavity producing peritonitis	Ureters and kidneys good
	52	4*	77	(1) 2-8-35 (2) 3-8-35	3-15-35	5 wks	Moderate infection of wound Early peritonitis right pyonephrosis	
	53	5	2 8	(1) 2-8-35 (2) 3-8-35	6- 1-35	5 mos	Bilateral hydronephrosis	

*Died of peritonitis
†Coffey method No III on right Left ureter was not implanted

tis (serial numbers 2 3 4, 5 10, 17, 29 41 and 48, Table II) In 3 of these the fecal leakage resulted from a slight necrosis of the bowel at the site of implantation and in 3 instances the sutures had failed to hold and the ureteral ends had slipped out of the bowel entirely All 4 dogs in which ureters were implanted directly (Fig 1), rather than obliquely by a submucous route, died of peritonitis In 3 of these there was gross leakage, in the fourth (No 1) an abscess at the site of the right implant Aside from the value of a submucous valve in the prevention of ascending infection an oblique insertion of the ureter undoubtedly secures a tighter anastomosis and lessens the danger of leakage and peritonitis The penetration of the lumen of the ureter by a suture caused urinary leakage in

1 dog (serial No. 27) which died of peritonitis Ten of the 13 instances of peritonitis, therefore resulted from leakage (of feces in 9 and of urine in 1)

C Infection of the abdominal wound Successful uretero-intestinal implantation in dogs is much more difficult than in man mainly because the ureter of the dog is smaller and has a much thinner wall In addition, infection of the abdominal wound occurs frequently in dogs in spite of strict asepsis. This infection comes from contamination of the wound from the inside when the bowel is opened and from the outside (skin) at the time of or after closure. A sterile dressing was not applied Twenty three of the 53 dogs had more or less severe infection of the abdominal wound and all died 4 of evisceration 8 of peritonitis, 9 of acute pyelonephritis, and 1 each of sepsis and pneumonia Two of the 5 dogs which were operated on by Higgins method died of peritonitis In 1 an abscess in the wound ruptured into the peritoneum after 28 days, producing peritonitis and the other died of peritonitis as a result apparently of contamination from the outside at the time the second stage of the operation was carried out

D Infection at the site of implantation This may present as a localized inflammation as part of a generalized peritonitis, or as a walled off abscess. The last condition occurred three times and was unassociated with peritonitis in 2 instances. Had these 2 dogs lived long enough, the local abscesses might have ruptured into the peritoneal cavity Undoubtedly this complication is the gravest of the dangers from contemporary contamination Infection about the ureter as it enters the bowel may produce peritonitis not only by direct extension but indirectly by causing localized necrosis of the bowel or ureter and the formation of a fistulous tract Direct extension seems to have been the cause of peritonitis in 2 dogs (Nos 45 and 52) The relation of inflammation arising from contamination and of necrosis resulting from suturing to the production of the localized sloughing which permitted leakage of the contents of the bowel, is uncertain Undoubtedly both are important factors

SUMMARY

1 Peritonitis rarely occurs as a result of contamination with the contents of the bowel or with urine at the time of operation when the obvious precautions are followed

2 Leakage from the bowel or the ureter after operation is the common cause of peritonitis

a Leakage occurs when the anastomosis is faulty and the ureter has not been sutured securely into the opening of the intestine. (An oblique submucosa insertion of the ureter is much safer than direct insertion)

b Leakage occurs when anchoring sutures tear or slough out (Sutures through serous and muscular layers of the bowel are insecure. The only safe layer for suturing is the submucosa, the use of which carries the greater risk of penetration of the lumen)

c. Leakage occurs when a suture punctures the bowel (fecal fistula) or the ureter (urinary fistula)

d. Leakage occurs with necrosis of a portion of the intestine or of the transmural portion of the ureter (The blood supply of the bowel or ureter must not be tied off by sutures or impaired by too great constriction, which may occur by suturing in layers)

3 Infection of the abdominal wound from contamination at the time of the operation is more imminent than peritonitis Abscesses in the abdominal wall may rupture to the inside and produce peritonitis. (The incision should be walled off more securely than the intestines are packed off and gloves, drapes, and instruments should be changed before closure is carried out)

4 Implantation, by any method which requires that the bowel be opened at the time, carries the considerable risk of localized inflammation both of the bowel and of the ureter A localized peritonitis may clear up or become general A local abscess may be absorbed or it may rupture into the cavity and then produce peritonitis A periureteritis may produce urinary obstruction or the infection may ascend to the kidney Localized inflammation may lead to anemic necrosis of the bowel or ureter which will permit leakage, and peritonitis will be the result. Inflammation at the site of implantation may result

from temporary leakage after operation, and probably this is the most frequent cause (The operative technique must prevent local contamination and secure a water-tight anastomosis)

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THE COURSE OF SINGLE MYELOMA OF BONE

A Report of Twenty Cases[1]

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THE question as to whether or not *myeloma of bone is a true tumor or a* generalized disease of the myeloid system has not been settled Most authors incline to the view that these lesions must be classified as true tumors

The term "multiple myeloma has arisen because these tumors spread very early and cases are *usually observed only in those stages* in which the disease is already generalized In order to support the opinion that myeloma is a true tumor following the course characteristic of tumors, the observation of cases with a solitary bone lesion with or without subsequent spread of the disease is very important Geschickter and Copeland *state* in their book as late as 1931 In only 5 cases (Wallgren Schmorl, Morax and Geschickter) has the disease been found in a single focus, and in all of these cases autopsy was not performed, although thorough roentgen ray studies were made in some"

This communication contains cases of myeloma collected from the literature which were proved either by necropsy or roentgen-ray findings to be single myeloma with or without subsequent spread of the disease In addition, the Bone Registry of the American College of Surgeons was studied and similar cases from this registry are included in this report It was necessary to eliminate from the literature those cases diagnosed as single myeloma in which the proof was not based upon roentgen or necropsy findings Among the cases to which Geschickter and Copeland refer we found it necessary to eliminate the cases of Morax and *Schmorl which were not* definitely single cases at the first observation The case reported by Lwald which is considered by some to be one of single myeloma we found necessary to eliminate because of the indefinite histological findings

We have collected from the literature 12 cases which in our opinion meet the requirements mentioned We have added to this group 5 cases which were found in a group of 75 registered as myeloma in the Bone Registry of the American College of Surgeons One additional single myeloma (Case 13) is added. Cases 19 and 20 are presented as problems in radiological differential diagnosis.

Case 1 Zdansky reports the case of a woman, age 68, who complained of joint pains of 1 year duration The patient had an intense albuminuria, secondary anemia, nephrosis, and thrombopenic purpura. Pain in the left leg was severe

X-ray reports In the upper third of the left femur there was an area of rarefaction, irregular in outline and 8 centimeters in length The cortex was thin and in some places completely destroyed "In other parts of the skeleton, lesions were not found roentgenologically A few days after these roentgenograms were taken, a spontaneous fracture of the femur occurred (The patient died shortly thereafter from heart disease)

Necropsy An amyloidosis of the heart and kidneys with shrinking of the kidneys was found A plasmocytoma was found at the site of the fracture of the left femur The central part of the tumor was destroyed by necrosis and hemorrhage The yellow *marrow was partly replaced by red marrow* in the long bones Histologically sections of the tumor showed plasma cells with many mitoses The histo*logical diagnosis was plasmocytoma* (Institut Marresch, Vienna)

The original communication presents a photograph of the femur with pathological fracture

This case presents a single tumor of the femur diagnosed *histologically as plasmocy*toma roentgenologically no other lesions could be found throughout the skeleton Concerning Bence-Jones protein nothing is mentioned in the report

Case 2 Geschickter reports the case of a woman, age 45 who complained of pain in the upper third of the left thigh of 2 months duration

Examination October 1929 (Dr Bloodgood) Clinically the patient had pain only in the left thigh Roentgenograms *of the left femur* revealed an area of bone destruction in the upper portion of the shaft at the site of the nutrient artery extending from the *intertrochanteric line to the beginning* of the middle third of the femur Cortical bone was intact without signs of periosteal destruction or reaction Roentgenograms *of the other long bones* the pelvis, spine ribs, and skull, were negative

[1] From the Tumor Clinic of the Michael Reese Hospital Chicago

Exploratory operation by Dr Bloodgood Unusual vascularity and hemorrhage were encountered under the periosteum The cavity seen in the X-ray film was cauterized A frozen section showed the tumor to be composed of sheets of cells resembling plasma cells Permanent sections confirmed the diagnosis of myeloma of the plasma cell type

Pathological fracture occurred shortly after operation

This case presents a plasma cell myeloma of the femur diagnosed by biopsy X-ray examination at the time of operation revealed no other lesions of bone Bence-Jones protein was not found

CASE 3 Wallgren reports the case of a woman, age 41, who in 1918 pulled two small fragments of bone from the posterior portion of the right upper jaw A few weeks later she observed a small, hard nodule at the site of the right upper second molar tooth On examination, the tumor was fluctuant There was a chronic tuberculosis of the right apex On X-ray examination there was found a defect in the alveolar process Skeletal X-rays revealed no other myelomas The urine contained Bence-Jones protein

The tumor was resected Histologically, it was composed of masses of small cells, alveolar in structure with many blood vessels containing large endothelial cells These vessels contained myeloma cells of the plasma cell type The histological picture was similar to other cases of myelomas reported by Wallgren

The case presents a tumor of the right upper jaw Histologically, plasma cell myeloma could be diagnosed from plasma cells found in the vessels These were of the same type as in other cases of multiple myeloma reported by the same author Bence-Jones protein was found in the urine Although the author is unable to arrive at the definite conclusion that this case is one of single myeloma, the presence of Bence-Jones protein with a single lesion and the histological finding of plasma cells support the assumption that this case is a single myeloma of the plasma cell type

CASE 4 Rogers presents the case of a man, age 34, who sustained a fracture of the right femur in November, 1927 In December, 1927, a second injury occurred at the same site following which swelling of the limb occurred

Examination June 21 1928 (Bristol General Hospital) There was a large fusiform swelling on the anterior inner aspect of the right thigh, firmly attached to bone and of seeming solid consistency X ray examination revealed a honey-combed appearance in the tumor mass and a rarefaction of bone extending above and below the site of the former fracture

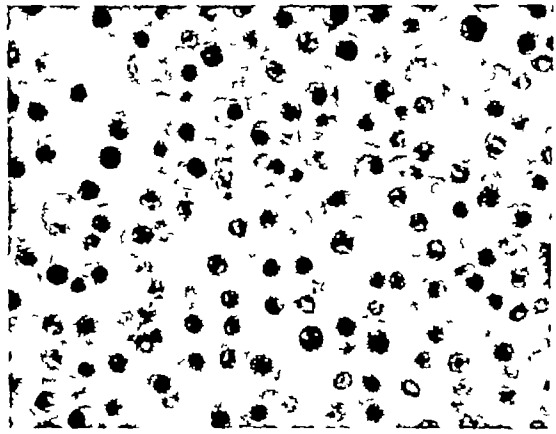

Fig 1 Solitary plasma cell myeloma of the femur (Case 10 Photomicrograph taken from the original section of the Bone Registry No 1438)

First operation June 22, 1928 Curettage The tissue removed was firm, grayish-white in appearance, and contained many areas of hemorrhage Microscopically, the tissue was composed of discrete polyhedral cells The pathological diagnosis was plasma cell myeloma

X-ray examination of the skeleton failed to disclose other foci of tumor formation The urine contained no Bence-Jones protein

July 3, 1928, radium needles were inserted in the cavity (150 mgm) and removed on the following day

The discharge of purulent fluid necessitated a second operation on November 27, 1928, with insertion of 140 milligram radium needles for 2 days and a third operation on January 8, 1929, at which time the cavity was filled with plaster of Paris On February 5, 1929, amputation through the upper third of the thigh was performed

According to a personal note received from the surgeon who performed the operation in this case (Professor Hey Groves), the patient was last seen on May 9, 1932, at which time he was in good health and without signs of recurrence or generalization

This case presents a single tumor in the femur which was first revealed following a fracture Histologically, the tumor proved to be plasma cell myeloma No other bones were involved Bence-Jones protein could not be demonstrated in the urine Following three curettages and final amputation, the patient has been well at least 4 years since the diagnosis of myeloma Amputation was performed 8 months after the original diagnosis

Fig Tumor of upper end of right femur t time of first observation (Case 14 Bone Registry N 7)

CASE 5 Shaw reports the case of a man, age 29, who sustained a fracture of the right humerus in the *middle third of the shaft One week after the fracture* a roentgenogram of the humerus revealed absorption and reticulation of bone at the site of fracture suggesting a central medullary tumor X-ray examination of all bones failed to reveal other lesions The humerus was exposed at operation and a soft medullary tumor at the site of fracture was removed by curettage. Microscopic examination of the tissue *removed at operation revealed an extremely cellular* tumor with extensive hemorrhage No multinucleated giant cells were present Pathological diagnosis was plasma cell myeloma. Several examinations of the urine after operation failed to show Bence-Jones protein Twelve months after fracture there was good union of bone and no evidence of recurrence of tumor

In a personal communication received from the author it is stated that the patient was last seen in 1931 at which time there was no evidence of local *recurrence or generalized myelomatosis*

CASE 6 Charbonnier and Mermod report the case of a woman age 6 who complained of pain in the *left hip* In August, 1932 the patient sustained a fracture of the upper third of the left femur following slight trauma Examination at this time disclosed a fracture of the upper third of the left femur The bone was rarefied and the cortex irregularly thin and cystic X-ray examination of the femur 1 month later showed progress of the disease

November 93 curettage was done Microscopic *examination showed tissue which consisted* entirely of plasma cells The histological diagnosis was myeloma An instructive photomicrograph is included.

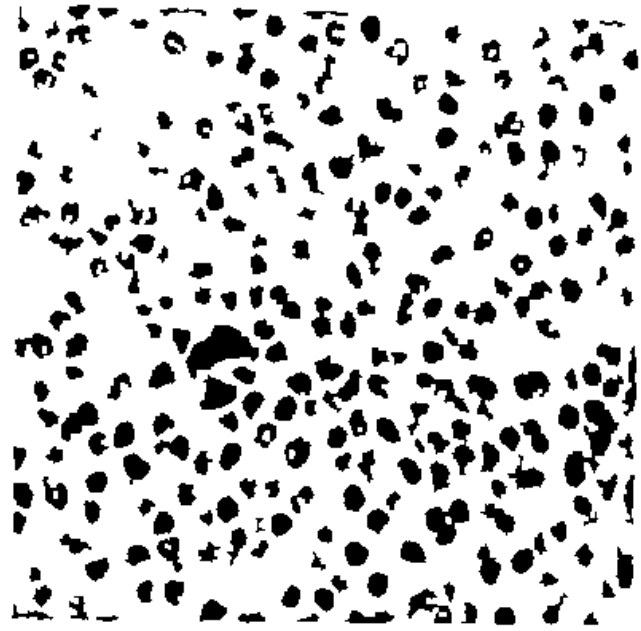

Fig 3 Photomicrograph Plasma cell myeloma Biopsy of the primary lesion of femur (Case 14 Bone Registry No 710)

Bence-Jones protein was not found in the urine *Following the operation, a fistula occurred in the* scar and a short time later a sacral tumor appeared which perforated into the rectum The patient became cachectic and on January 15, 1933, died of cachexia

Necropsy (Askanazy) did not show other skeletal tumors in spite of a very careful examination (skull, ribs, sternum, pelvis, spine, long tubular bones of the *extremities*) The *histological* postmortem diagnosis was solitary myeloma of the plasmocytoma type

The anatomical findings in this case are extensively reported by Rutishauser *This author calls special* attention to the infiltrative character of the tumor For this reason, Askanazy proposes the term myelosarcoma for this case

This case presents a solitary tumor in the upper third of the femur which was diagnosed histologically as plasma cell myeloma Bence-Jones protein was not present *No other parts* of the skeleton were involved

The striking feature of this case is the malignant course and rapid growth of the solitary tumor From the reproduction of some of the X ray films, one might diagnose osteogenic sarcoma The entire course of the disease from the first diagnosis to death was only 6 months.

CASE 7 Walthard presents the case of a man, age 55, who in August 1922 noted pain in the back of *the neck* In May 1923 the patient experienced difficulty in walking, with symptoms denoting compression of the spinal cord below the first dorsal segment.

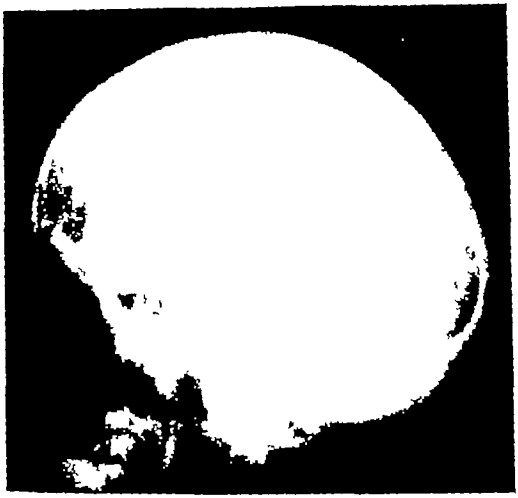

Fig 4 X ray of skull December 31, 1923 Made at time of original observation of the tumor of the right femur No visible lesion in the skull (Case 14 Bone Registry No 710)

Fig 5 X-ray of skull September 24, 1926, at the time of generalization of the disease Three years after original observation of primary tumor (Case 14 Bone Registry No 710)

In June, 1928, a laminectomy was performed and the patient died after operation

At necropsy destructive lesions of the first thoracic vertebra and the seventh cervical vertebra were found The tissue was grayish-red and hemorrhagic The histological findings revealed plasmocytoma, the cells of which contained the typical spoke-like nuclei

Bence-Jones protein was not reported There were no lesions in the other bones

Fig 6 Lesion of the femur 3 years after original observation of myeloma (Case 14 Bone Registry No 710)

This case presents a tumor which had destroyed two vertebræ, and which was diagnosed microscopically (Hedinger) as plasmocytoma The patient died after operation The invading character of this tumor is noteworthy A photomicrograph is included

CASE 8 Mathias presents the case of a man, age 65, who had observed a slowly growing tumor of the right parietal area The tumor was widely excised Histological examination showed a myeloma with cell structure of plasmocytoma The patient had

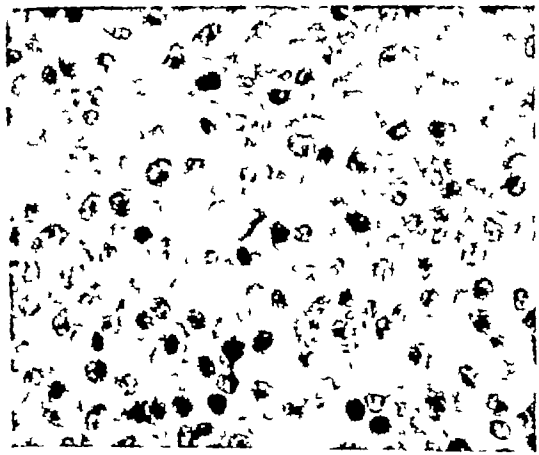

Fig 7 Plasma cell myeloma of humerus. (Case 15 Bone Registry No 1597)

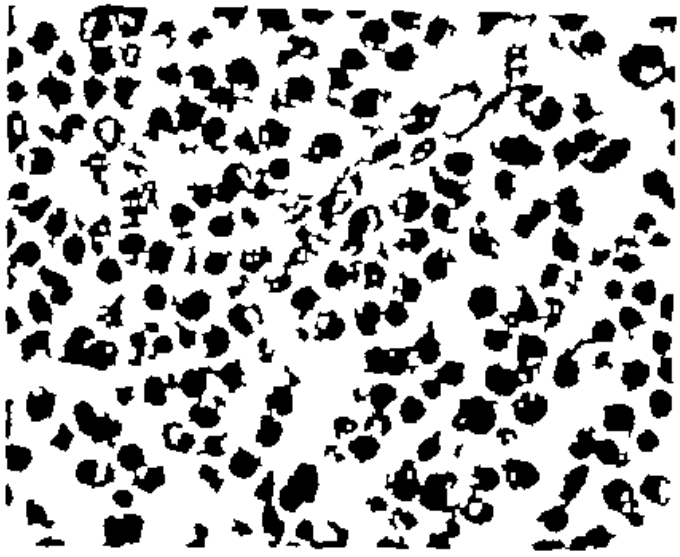

Fig 8 Photomicrograph Plasma cell myeloma of the ilium (Case 6 Bone Registry No 1148)

Fig 8a Myeloma of the ilium ith roentgenographic appearance of giant cell tumor (Case 6 Bone Registry N 148)

been *free of disease 18 months at the time of the report During the observed course of the disease,* no other bone involvements had been noted Bence Jones protein was not found in the urine

CASE 9 Cabot presents the case of a man, age 33, who was admitted to the Massachusetts General Hospital acutely ill The patient had neurologic signs of compression of the spinal cord at the level of the fourth thoracic vertebra

Laminectomy was performed, at which time a grayish mass was found at the level of the fourth dorsal vertebra *which did not invade the dura* The patient subsequently died

The patient was found to have infarcts and abscesses of the right lung with hemorrhagic cystitis Primary myeloma of the bone marrow in the fourth dorsal vertebra was found. *At the post mortem examination no tumor was found anywhere else in the body*

Regarding the histology of this tumor Dr Tracy B Mallory states "I think, however there is no question but the tumor has to be classified in the general group of myeloma I mean by that simply a primary tumor of the bone marrow which is not the typical plasma cell myeloma and we are not able to decide which of the various other types it is In some areas it shows cells suggesting plasma cells, in *other areas extraordinary numbers of multinucleated* giant cells suggesting strongly a tumor of megakaryocytes.

CASE 10 Bone Registry of the American College of Surgeons Case Number 1438

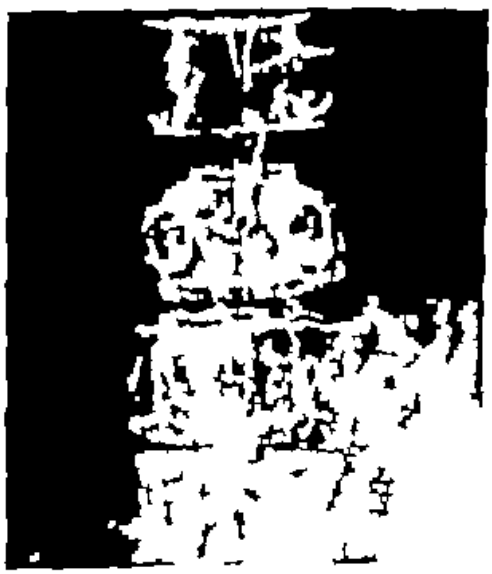

Fig 9 Destructive lesion of second lumbar vertebra (Case 8 Bone Registry N 67)

Fig 10 Destructive lesion of second lumbar vertebra 6 years after Figure 9 Histologically the lesion is plasma cell myeloma (Case 8 Bone Registry N 67)

Fig 11 Destructive lesion of the eighth thoracic vertebra. Microscopically plasma cell myeloma (Case 10 Michael Reese Hospital Tumor Clinic No 2147)

Harding and Kimball report the case of a man, age 60, who in January, 1930, complained of a dull aching pain in the region of the left hip which radiated down to the knee In June, 1930, pathological fracture of the femur at the level of the lesser trochanter was found The radiographic appearance was that of a purely osteolytic lesion and was confined to the region of the fracture

Examination July 19, 1931 (Los Angeles County General Hospital) Radiographic examination of the entire skeleton showed the lesion to be limited to the left femur At the level of the lesser trochanter there was an area of rarefaction with a widening of the adjacent shaft The medullary cavity was more extensively involved than the cortex

The urine was negative for Bence-Jones protein

In September, 1931, a disarticulation of the leg at the hip joint was performed, and the patient died in surgical shock.

Examination of the removed extremity showed a tumor 7 centimeters in diameter occupying the medullary cavity which had produced a destruction of the cortex of the femur and had invaded the muscles of the thigh The microscopic picture (Fig 1) was characteristic of plasma cell myeloma The pathological diagnosis was plasmocytoma of the femur

Careful examination of the other bones at necropsy failed to disclose other foci of tumor

This case presents a solitary plasmocytoma of the femur with pathological fracture The

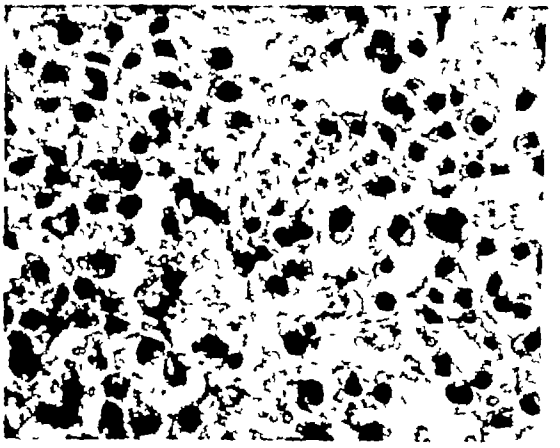

Fig 12 Plasma cell myeloma (Case 10 Michael Reese Hospital Tumor Clinic No 2147)

patient died in surgical shock after disarticulation 15 months after the lesion was first observed roentgenologically and 20 months after the first subjective symptoms had developed Examination of the skeleton both by X-rays during life and at necropsy failed to show other lesions The urine contained no Bence-Jones protein

A remarkable feature in this case is the invasive character of the tumor The case is accepted by the Bone Registry of the American College of Surgeons as plasma cell myeloma

CASE 11 Bloodgood reports the case of an adult male who had sustained trauma to the right shoulder Thirteen months later swelling appeared in the outer third of the clavicle

X-ray examination demonstrated a uniform expansion of the medullary cavity of the outer third of the clavicle in which only a very thin shell of bone was preserved The X-ray film revealed a lesion resembling a bone cyst or a giant cell tumor No other skeletal X-rays were taken prior to operation

No examination of the urine for Bence-Jones protein was made before the operation

In view of the rapid growth and very thin bony shell, resection was performed The tumor consisted of a whitish mucoid material with hemorrhagic areas Frozen sections gave the appearance of round cell sarcoma and contained cells characteristic of myeloma

After operation, Bence-Jones protein was found in the urine

X-ray studies of the other bones of the skeleton were negative until some 2 months after operation at which time a second bone focus was found in one of the ribs

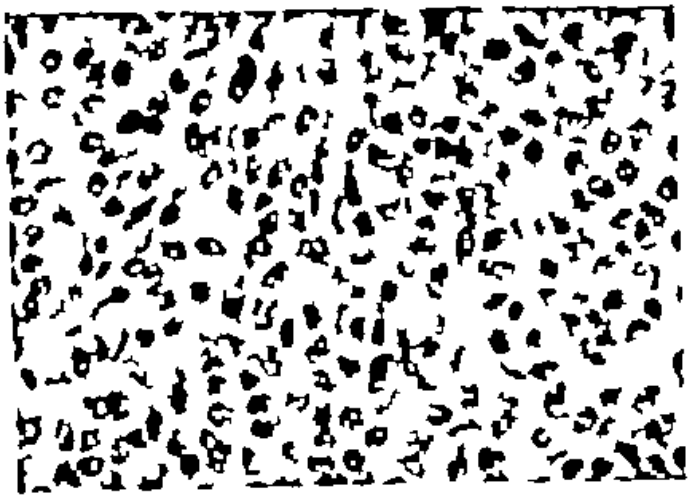

Fig 3 Plasma cell myeloma of the femur (Case 10 Bone Registry No 1)

This case presents a tumor in the outer third of the right clavicle histologically diagnosed as myeloma. Skeletal X-ray films showed no other lesions until 2 months after operation The urine contained Bence Jones protein in large quantities even before generalization of the disease was observed

CASE 11 Peyton presents the case of a man, age 49, who began to have pain in the region of the xyphoid process radiating across the upper abdomen 1 year prior to the first examination. Weakness developed in both legs 4 months prior to examination

Fig 5 As further demonstration of the difficulties encountered in the roentgenological diagnosis of myeloma, we present an X ray film of the chest taken of patient with typical, multiple generalized myelomas proved by biopsy Bence Jones protein was present in the urine This film reveals typical discrete punched out lesions in the ribs as well as a lesion in the outer third of the right clavicle which, if seen by itself might lead one to the diagnosis of giant cell tumor of the clavicle from the roentgenological appearance alone (This picture was obtained through the courtesy of the Edward Hines Hospital of the United States Veterans' Facility Hines, Illinois)

Fig 14 Roentgenogram of the right femur showing bone destruction with cortical expansion Roentgenological diagnosis, giant cell tumor Histological diagnosis, plasma cell myeloma (Case 10 Bone Registry No 1101)

Examination July 1930 The X-ray films showed the sixth thoracic vertebra to be compressed and rarefied and the intervertebral disc between the fifth and sixth thoracic vertebrae to be almost obliterated X-ray films of the lungs and ribs were negative The urine was not tested for Bence-Jones protein

Treatment On September 3, 1930, laminectomy was done The sixth thoracic vertebra and the head and neck of the sixth rib were replaced by tumor The dura and cord proper were not invaded, although surrounded and compressed by tumor Eleven radium needles (65 milligrams total) were inserted into the tumor mass and left in place for 20 hours, giving a total dose of 1300 milligram hours Filtration of 0 5 millimeter nickel steel was used

Microscopic examination of the tissue removed at operation revealed small round cells with hyperchromatic nuclei and with an occasional mitotic figure The pathological report was plasma cell myeloma

After operation the patient received external X-ray therapy in four treatments over a 6 day period Through an anterior and a posterior portal, the patient received 132 per cent skin erythema dose to each portal with 200 kilovolts, 1 millimeter copper + 1 millimeter aluminum, at a skin target distance of 50 centimeters One year later a second series of X-ray treatments was given.

The patient could walk following operation Skeletal X ray examination in March 1937 did not reveal additional lesions The urine at this time con-

tained Bence-Jones protein In February, 1934, the patient was still living but had generalized metastases of the skeleton The patient died in March, 1934.[1]

This case presents a primary myeloma of the vertebra with no other skeletal involvement over a period of 19 months Generalized myeloma followed the primary tumor The urine was not examined for Bence-Jones protein in the early stages After the disease had become generalized, Bence-Jones protein was present

CASE 13 [2] This patient was a woman, age 38, who received an injury to the left parietal bone in October, 1928 In December, 1928, she observed a soft swelling over this area which was not tender or painful

In March, 1929, the patient was examined at the Mayo Clinic At this time a large, cranial defect was found in the left parietal bone, replaced by a soft pulsating mass No other rarefactions were noted in the skull, spine, ribs, chest, or sternum The blood count was normal, the Wassermann, negative Blood calcium was 9 9 milligrams per cent The patient received X-ray therapy over the tumor

In April, 1929, the tumor had disappeared The patient complained of pain in the left shoulder Skeletal X-ray films were still negative Bence-Jones protein was present

In May, 1929, skeletal X-ray films revealed numerous punched out areas throughout the skull Bence-Jones protein was again present The patient received additional X-ray therapy

In January, 1930, the patient sustained a fracture of the left humerus which healed in 6 weeks At this time hemoglobin was 29 per cent The patient complained of pain in the joints, chest, and extremities

In March, 1931, the patient was admitted to University Hospital (Minnesota) Skeletal X-ray examination revealed many areas of rarefaction with pathological fractures of several of the ribs and of the pubes Roentgenological findings were characteristic of multiple myeloma The urine contained large quantities of Bence-Jones protein The patient died on March 4, 1931, of intestinal obstruction after an appendectomy had been performed

Postmortem (abdominal only) The abdomen contained about 500 cubic centimeters of bloody fluid No evidence of mechanical obstruction was found The lower ribs were thickened and were the site of several fractures The iliac bones were soft and friable Marrow obtained from the ribs and iliac bones gave the characteristic appearance of plasma cell myeloma

The first observation of this case 4 months after the onset of the symptoms revealed a lesion in the left parietal bone only One month later, skeletal X-ray films revealed no other lesions At this time Bence-Jones protein was present One month later (2 months after the first observation and 6 months after the appearance of the primary tumor) generalized metastases to the skull could be demonstrated The patient lived 2 years and 4 months after the diagnosis of the primary lesion and 1 year and 9 months after generalization occurred Histologically, plasma cell myeloma was found at necropsy

CASE 14 Bone Registry of American College of Surgeons Case Number 710

Patient was a male, age 56, who at the age of 21 was injured in a railroad accident. Paralysis of the lower extremities was present following this accident The patient recovered and was apparently well until the age of 56, at which time there was slight pain in the right upper thigh in the region of the greater trochanter One month later X-ray films showed a bone tumor of the upper end of the right femur (Fig 2[3]), intramedullary in position The lesion was considered to be a giant cell tumor X-ray examination of the other bones revealed no further lesions

The urine contained no Bence-Jones protein

In January, 1924, curettage was done, at which time fracture of the femur occurred The extremity was placed in Buck's extension Microscopic examination of tissue revealed typical plasma cells in various stages of mitosis Diagnosis was myeloma of the plasma cell type (Dr A A Eggston, Dr F Parker, Jr, Dr F B Mallory, and Dr J Ewing), (Fig 3)

In December, 1925, the patient was in excellent general condition In September, 1926, generalized metastases were observed (Fig 5[3]) The patient died in 1926 shortly after the accompanying photographs (Figs 5 and 6[3]) were made Bence-Jones protein was found in the urine prior to death

This case presents a single myeloma of the right femur diagnosed microscopically as plasma cell myeloma The exact interval between the diagnosis of the primary tumor and the later generalization cannot be determined Two years after the discovery of the primary tumor, the patient was still in excellent health He died 3 years after the original diagnosis had been made Bence-Jones protein, which was not found in the early stages of the disease, was demonstrated prior to death

CASE 15 Bone Registry of American College of Surgeons Case Number 1597 Patient was a man, age 57, who in May, 1932, sustained trauma to right shoulder with fracture

[1] Information regarding the subsequent course of the disease was received from Dr W T Peyton

[2] This case was reported to us in a personal communication from Dr W T Peyton

[3] X-ray films reproduced here were obtained through the courtesy of Dr Joseph E. J King

In December 1932, X-ray examination (Out Patient Department of the Vanderbilt University Hospital, Nashville) showed a destructive lesion in the proximal portion of the right humerus. A complete destruction was found just below the head of the humerus with pathological fracture and extension into the soft tissues. The impression was that of a sarcoma of the humerus

In May, 1933, the presence of Bence-Jones protein was questionable at first examination. On repeated examinations Bence-Jones protein was absent. X ray examination at this time revealed a complete destruction of the medulla and cortex and invasion of the soft tissues. X-ray examination of the skull, pelvis, and chest revealed no other lesions

A resection of the proximal end of the humerus was done. At operation the tumor seemed to be entirely enclosed by normal periosteum. The tumor tissue was composed of dark red, friable material which, microscopically was composed of closely packed cells resembling plasma cells. Mitotic figures were common. No giant cells or no new bone formation could be seen (Fig 7) The original pathological diagnosis was myeloma, although not a typical plasma cell type. Subsequent diagnosis of plasma cell myeloma was made by Drs Crowell, Hartman, Morton, Warren, Lebowitz, and Simmons

In September 1933 numerous small areas of increased penetration through many of the ribs were found by X-ray examination In May 1934, X-ray examination revealed increased penetration over the wing of the left ilium and near the acetabulum on the right. The right scapula and many of the ribs showed small areas of increased penetration suggestive of multiple myeloma. In October, 1934 both clavicles and many of the ribs showed areas of increased penetration varying in size.

Bence-Jones protein was found in the urine for the first time.

In November 1934, the patient received X-ray therapy (total 1900 r)

The patient died in April, 1935.

This is a case report of a single myeloma of the humerus associated with pathological fracture. At the original examination no other bones were involved, and the urine was negative for Bence-Jones protein. The first signs of generalization were found 10 months after the diagnosis of the primary lesion was made, and 17 months after the first fracture occurred Bence-Jones protein was found in the urine for the first time 23 months after the first diagnosis.

CASE 16. Bone Registry of the American College of Surgeons Case Number 1148

This patient was a woman, age 39, who was admitted to St Michael's Hospital in Toronto Two years prior to first examination, the patient developed pain in the left hip which was diagnosed as sciatica. In January 1928, there was pain radiating from the left hip to the left knee upon movement. Upon admission to the hospital there was a round, firm swelling over the left anterior superior spine of the ilium, and marked atrophy of the muscles of the left lower extremity

In August, 1928, a biopsy of the tumor was done (Fig 8) The pathological diagnosis was plasma cell tumor (myeloma) Bence-Jones protein was found in the urine at this time. Subsequent X-ray examination of the skeleton did not reveal other lesions. X-ray examination of the left ilium showed a large tumor of the ala, having the radiographic appearance of a giant cell tumor (Fig 8a)[1]

In February 1929, the patient received X-ray therapy

In June, 1930, the patient died.

At necropsy myeloma of the left ilium was found. In addition there were pulmonary abscesses and a chronic nephritis. Gross examination of the skeleton at necropsy revealed no evidence of tumors in other bones.

This case presents a single myeloma of the left iliac bone. The sections show a myeloma of the plasma cell type (Drs. Crowell, Codman, Simmons, Stewart, Copeland, and Magner) Neither X-ray examination during the life of the patient nor gross examination at necropsy revealed any evidence of tumors in other bones. Bence Jones protein was positive in the urine in a comparatively early stage. The patient died with symptoms referable to a chronic nephritis. Unfortunately the clinical analysis from the point of view of the nephropathy does not indicate whether the kidney changes are referable to the metabolic disturbances associated with Bence-Jones proteinuria (myelomatous nephrotic contracted kidney) From the literature and in our own experience, typical changes in the kidneys have been observed only in the generalized state of the disease. Therefore, this case would be very important from the point of view of the relation of the metabolic disturbances and the extension of the bone disease More clinical and pathological data in regard to the kidney pathology in this case would be pertinent to the relation between Bence-Jones proteinurea, kidney changes, and the stage of generalization of the disease.

The following information was obtained through the courtesy of Dr A M Wanless.

[1] This X ray film was obtained through the courtesy of the X ray Department of the St Michael Hospital, Toronto, Canada

CASE 17 Bone Registry of American College of Surgeons Case Number 1195

A man, age 58, was admitted on the Genito-Urinary Service of the Massachusetts General Hospital with prostatic obstruction X-ray examination taken on this occasion revealed a large area of diminished density with trabeculation in the right ilium Biopsy showed plasma cell myeloma

In March, 1931, general skeletal roentgenograms were negative X-ray therapy was given

In May, 1931, general condition was excellent X-ray examination of the pelvis showed some filling in of new bone and expansion of the process

In August, 1932, the condition remained the same

This case presents a single plasma cell myeloma of the right ilium (Drs Crowell, Codman, Stewart, Simmons, Broders, Meyerding, Brooks) There were no signs of involvement of other bones Bence-Jones protein was not reported The patient was well 20 months after the first observation of the tumor

CASE 18 American College of Surgeons Bone Registry Case Number 1167

A Negro man, age 52, was admitted to the Massachusetts General Hospital in December, 1924 His chief complaint was pain in the right leg following an injury The X-ray examination revealed a destructive lesion of the body of the second lumbar vertebra The diagnosis was giant cell tumor

In August, 1930, the condition of the patient was more acute At this time there was vertebral compression The patient was given X-ray therapy without noted improvement

In December, 1930, a stabilizing operation was done Microscopic diagnosis of tissue removed at this time was plasma cell myeloma

Complete skeletal X-ray films taken later showed no other bone involvement The urine showed no Bence-Jones protein

In September, 1932, the patient's general condition was good, but the disease had extended to adjacent vertebræ

In August, 1934, the condition remained unchanged

This is a case report of a single myeloma of the vertebra which was diagnosed as plasma cell myeloma (Drs Crowell, Ewing, Stewart, Simmons, Codman, Hartwell Hartman, and Broders) The skeletal X-ray films revealed no other foci of bone involvement 6 years after the first observation Bence-Jones protein was not found in the urine Eight years after the original observation the process had extended to adjacent vertebræ At the patient's last examination the disease had been observed over a period of 10 years, and at that time was still present in the original vertebra and the adjacent vertebræ

CASE 19 A Negro man, age 56, in December, 1934, noted the onset of sharp, shooting pains radiating from the perineum down both lower extremities Progressive weakness and stiffness of both lower limbs developed until June, 1935, when he became completely bedridden In June, 1935, he was admitted to the Michael Reese Hospital, at which time he had a spastic paraplegia There was marked adductor spasm Loss of cutaneous sensation was found on the left side up to the level of the tenth thoracic segment, and on the right side to the twelfth thoracic segment There was bilateral exhaustible ankle clonus Knee and ankle jerks were bilaterally brisk and equal There was a bilateral positive Babinsky Proprioceptive sensation was present in feet and ankles The cremasteric and abdominal reflexes were bilaterally absent There was a positive Beevor's sign The upper extremities and cranial nerves were normal

A diagnosis of spinal cord neoplasm at the level of the ninth, tenth, and eleventh skin segments was made The urine was not examined for Bence-Jones protein

X-ray examination (Fig 11) of the spine showed a rarefaction of the bone of the eighth thoracic vertebra The bone outline was practically intact, but the general appearance was that of a destructive lesion of the eighth thoracic vertebra

Operation by Dr David Cleveland, June, 1935 A laminectomy was done over the fifth, sixth, and seventh vertebræ Laminæ of the sixth and seventh vertebræ were softer than normal The spinous processes of the sixth and seventh vertebræ were undermined by a soft, gelatinous reddish-brown tumor mass The spinal cord was completely covered in the region of the fifth, sixth, and seventh thoracic vertebræ by this soft tumor tissue which extended completely around the cord and upward beneath the lamina of the fourth thoracic vertebra Because of the widespread involvement, it was deemed surgically unwise to do more than decompression of the cord over this area Microscopic examination of tissue removed at operation revealed a myeloma of small round cells with darkly staining eccentric nuclei A diagnosis of plasma cell myeloma was made (Dr Max Cutler), (Fig 12)

X-ray examination of the skull, chest, and femora taken 6 weeks after operation revealed no evidence of other lesions of bone In the left ilium there was a sharply outlined area of rarefaction about 0 5 centimeter in diameter, which was probably an early secondary focus

The urine was repeatedly negative for Bence-Jones protein

This case cannot be presented as one of single myeloma because X-ray films taken 6 weeks after operation revealed a questionable

TABLE OF CASES

Case No. Sex Age	Location of primary tumor	Bence Jones present: Early stages	Bence Jones present: Later stages	Time from onset of symptoms (onset to first observation)	Complicating period and observations by time of case report	Time from primary tumor to death	Living	Treatment	Length of later (general health)	Remarks	Source of material
F 46	Femur (upper third)	?	?	yr	Observed only short time (days)	Short time (days)			R G	Associated malignancy with [illegible] metastasis, [illegible] purpura, and secondary chronic	Lansky
F 43	Femur (upper third)			mos.	?			Biopsy	R G	Postmenopausal pathological fracture	Gundersen
F 7	Mandible	+		7 yr 9 mo	?			Extraction	R G		Wallgren
M 24	Femur			7 mos.	4 yrs		4 yrs (not had spread up longer)	Curettage, radium, prolonged complication	R G	Pathological fracture. Radiographic appearance of giant cell tumor	Rogers
M 20	Humerus (scapula)			wk			9 yrs	Curettage	R G	Pathological fracture	Shaw
F 46	Femur (upper third)			Several mos.	6 mos	6 mos		Curettage	N G	Pathological fracture. Malignant sarcomatous tumor	Charbonnier and Marcand, Rich [illegible]
M 23	Vertebrae (7th cervical or thoracic)	?	?	20 mos				Laminectomy and curettage	N G	Invasive tumor. Patient died postoperatively	Wahlund
M 45	Skull (parietal)			?	18 mos		18 mos	Excision	S		Mathers
M 32	Vertebra (4th thoracic)	?	?	4 wks	?	?		Laminectomy	N G		Colmer-Hulme
F 46	Femur (upper third)			6 mos	mos.	mos.		Diverticulotomy	R N S	Pathological fracture. Radiographic appearance of giant cell tumor	Hardwicke, Lambert, Bone Reg. 1877 [illegible]
F 30	Ilium	+		yrs.	3 mos	12 mos		X ray	R N S	Associated chronic nephritis. Radiographic appearance of giant cell tumor	Bone Registry [illegible]
M 24	Ilium	?	?		yr 7 mos.		yr 7 mos	Biopsy	R G		Bone Registry [illegible]
M 1	Vertebra (2d lumbar)			?	10 yrs		10 yrs	X ray, stabilizing operation	R G	Radiographic appearance of giant cell tumor	Bone Registry [illegible]
M adult	Clavicle (entire) (head)	++		12 mos	mos.*	?		Extraction	O	Radiographic appearance of giant cell tumor. One normal [illegible] later at [illegible]	Blundell
M 40	Vertebra (6th thoracic)	?		yr	19 mos.*	4 yrs		Laminectomy (through, by [illegible]) + X ray therapy	O	Osteoblastic occurred between 10 months and 4 years after observation of primary tumor	Payne
F 36	Skull (parietal)	+	+	3 mos	3 mos.*	3 yrs. mos		X ray	O		Payne
F 46	Femur (upper third)		+	mos.	yrs. 9 mos.*	About 3 yrs		Curettage	O	Radiographic appearance of giant cell tumor	Bone Registry [illegible]
M 17	Humerus (proximal third)		+	mos.	9 mos.*	yrs 4 mos		Extraction, X ray	O	Pathological fracture	Bone Registry [illegible]

*Time from first observation to generalization.
(?) indicates generalization, + indicates simple lesion, M indicates that the case was proved by necropsy, R indicates that the other lesion was confirmed roentgenologically.

TABLE OF CASES

Case Sex Age	Location of primary tumor	Bence Jones protein		Time from onset of symptoms to 1st observation	Complete period of observation to time of case report	Time from primary tumor to death	Living	Treatment	Single or later generalized†	Remarks	Source of material
		Early stages	Later stages								
19 M 56	Vertebræ (4-8 thoracic)	0	0	6 mos*			8 mos to date	Radiation treatment in progress Laminectomy		Patient under therapy at present time. Questionable secondary focus left ilium	Michael Reese Hospital Tumor Clinic No 2147
20 F 50	Femur (upper third)	?	?	2½ yrs		6 yrs. 9 mos.		Biopsy		Radiographic appearance of giant cell tumor Questionable secondary focus was present in lower dorsal vertebræ This case is presented for differential diagnosis	Bone Registry 1101

*Time from first observation to generalization
†G indicates generalization S indicates a single lesion, N indicates that the case was proved by necropsy R indicates that the other bones were examined roentgenologically

secondary lesion The case is presented because of the striking similarity of the primary tumor to those in Cases 7, 9, 12, 18 At the present time the patient is receiving radiation therapy to the primary lesion

CASE 20 American College of Surgeons Bone Registry Case Number 1101

This patient was a woman, age 50, who, about 2½ years prior to first examination, sustained a fracture of the hip Function was regained but a tumor mass appeared at the site of fracture

In July, 1926, the patient was operated on (Hospital for Joint Diseases, New York City) Microscopic examination of tumor tissue removed (Fig 13) showed plasma cells A diagnosis of plasma cell myeloma was made

In August, 1926, the patient was admitted to the Memorial Hospital in New York City X-ray examination (Dr Herendeen) revealed a tumor causing bone destruction of the neck and greater trochanter of the right femur at the upper end of the shaft The cortex was expanded and the trabeculated appearance suggested a giant cell tumor (Fig 14)

X-ray examination of the chest in October, 1926, was negative An X-ray film of the spine revealed evidence of bone involvement in the lower dorsal vertebræ

In October, 1928, the patient's general condition was good

In April, 1933, the patient died at her home Cause of death is unknown

A diagnosis of plasma cell myeloma was made from sections obtained at the first operation, and confirmed by the following pathologists of the Bone Registry of the American College of Surgeons Drs Morton, Ewing, Stewart, Copeland, Codman, Simmons, Hartwell, Coley, and Curphey All emphasize the striking discrepancy between the radiological findings suggesting giant cell tumor and the histological findings of plasma cell myeloma

This case presents a problem in diagnosis between the radiographic findings suggestive of giant cell tumor and the histological evidence of plasma cell myeloma Bence-Jones protein is not reported Thorough skeletal X-ray examination was made which revealed evidence of bone involvement in the lower dorsal vertebræ

Although unable to classify this case as one of single plasma cell myeloma, we include it because of its diagnostic interest It will be noted that other cases herein reported give radiographic evidence of giant cell tumor which, nevertheless, were proved histologically to be plasma cell myelomas

RÉSUMÉ OF CASES

These cases of solitary myeloma may be separated into two groups, the first group comprising those cases in which the disease started as a single lesion and subsequently became generalized, and the second group comprising those cases in which the lesion remained solitary during the entire period of observation, either until death or until the time of the original report

The first group (a solitary lesion later becoming generalized) is more important in support of the view that all so called multiple myelomas arise in a solitary focus and become generalized, and that only the rapidity of spread produces the clinical picture of multiple myelomas as it is usually seen

The time interval between the definite diagnosis of a single myeloma and the later

proof of metastasis ranged from 2 months to 2 years 9 months (in the 5 reported cases 2 months, 5 months 9 months 19 months 2 years 9 months) In the case with the longest interval, the patient was treated by curettage of the primary lesion. This case will be discussed separately inasmuch as the clinical and roentgenological signs are typical of a giant cell tumor

In Case 12 we know only that the patient was still without metastases after 19 months and that the patient died with generalized metastases 4 years after the primary tumor had been discovered. This case was treated by laminectomy followed by interstitial radiation (1300 milligram hours) and external roentgen therapy

The duration of life following the onset of generalization was 1 month 19 months, 29 months, 35 months. The primary focus in each case was clavicle, vertebra, skull femur and humerus. In 2 of the cases of this group Bence Jones protein was found in the urine at the time of the solitary lesion In 2 cases it was found only after the condition had become generalized.

The second group (cases remaining solitary) contains 13 cases. Four of these patients were dead at the time of the original report. Two of them died 6 and 23 months after the first observation. Two died in surgical shock Case 6 with a duration of life of 6 months, was treated by curettage of the femur This case was diagnosed histologically (Askanazy) as myelosarcoma because of the malignant invading character of the growth. Five patients of this group were alive at the time of the original report, and by follow-up information it was determined that the duration of life since the first observation has been 12 months 18 months, 1 year 7 months, 4 years 10 years

We call attention to the fact that 2 cases with long duration—considerably longer than the average course of this disease—received intense treatment One of them (Case 4) was treated by curettage followed by interstitial radiation and subsequent amputation At the time of the last examination (4 years after operation) the patient was alive and well, without signs of recurrence or generalization of the disease The other case (Case 18) was originally treated by X-ray therapy followed by a stabilizing operation. One patient died only a few days after the original observation. We cannot draw any conclusions from this case, since the patient came under observation in a cachectic state with severe anemia, nephrosis, and thrombopenic purpura. In 3 cases of this group, we do not know the subsequent course of the disease.

In a recent editorial of the *Journal of the American Medical Association* attention is called to a group of myelomas exhibiting solitary lesions. The benign nature of solitary lesions is emphasized. The cases reported in our communication seem to indicate that we can go one step further and recognize two groups of solitary myelomas. One group is solitary only in the beginning and subsequently becomes generalized. The prognosis in this group does not differ from that of multiple myeloma. The second and rare group, may be called true solitary tumors A prolonged observation (4 to 10 years) proves that they remain local

The question arises as to whether all of the lesions which remained single belong to the same pathological entity Cases of the first group show only that it has been possible to recognize a primary single lesion and observe its generalization. Some of the cases of the second group raise the question of whether the lesions remained single because the time of observation was not sufficiently long to observe a subsequent generalization This objection may be applicable to Cases 1 2 6 7, 8 9, 10, and 17 In Cases 4, 5, and 18 with a duration of 4, 9 and 10 years, respectively the time is long enough to assume that these cases will not become generalized. In seeking a reason for this we may ask whether the long duration is due to the treatment received. It is unlikely that the duration as a single lesion in Case 18 was due to the treatment because the lesion did not respond to radiation. Whether or not Case 4, treated by curettage, radium puncture, and finally amputation was cured by this treatment cannot be decided from this case alone.

It is of interest to note that the clinical and radiological appearance in Cases 4 and 18 was that of a giant cell tumor In both of these

cases, however, the diagnosis of plasma cell myeloma was made by competent pathologists On the other hand, we may note that this appearance of giant cell tumor in the radiological picture was shown not only in the 2 cases mentioned but also in 2 others (Cases 9 and 10) In 1 of these cases (Case 10) this radiological picture was accompanied by the histological findings of a malignant infiltrating growth differing from the typical picture of plasma cell myeloma Furthermore, it may be noted that one of the single lesions which later became generalized (Case 14) likewise showed the clinical and radiological appearance of giant cell tumor and was curetted under this diagnosis

Because of the interesting behavior of some of these tumors which show the clinical and radiological characteristic of giant cell tumor, and which nevertheless were proved histologically to be myeloma, we have included Case 20 in this report An additional roentgenogram (Fig 15) showing this discrepancy in radiological appearance in the same chest is presented In the original findings of Case 20, with the radiographic appearance of giant cell tumor, the suspicion arose that a metastasis had already occurred If this were true, this case would be very similar to Case 14 in its course From these findings, there may be reason to believe that such cases have a different biological course from the typical plasma cell myelomas However, the material herein presented is insufficient to do more than point out this possible variation

SUMMARY

Eighteen cases of solitary myeloma of bone are reported, 12 cases from the literature, 5 from the Bone Registry of the American College of Surgeons, and 1 additional case Two cases are presented as problems in radiological diagnosis

In 5 cases the myeloma was solitary at the first observation and later became generalized This is the behavior that is common to other types of malignant tumors The only peculiarity of myeloma is the affinity for the osseous system which may be compared to the affinity of lymphosarcoma for the lymphatic system

In 13 cases there was no generalization of the disease during the time of observation In 7 cases the duration of the follow-up (longest duration 1 year and 7 months) is too short to permit the conclusion that these cases would not have become generalized Two patients with observed myeloma 4 and 10 years were alive without generalization at the time of the report

The location of the primary tumor was found in the clavicle in 1 case, in the maxilla in 1 case, in the humerus in 2 cases, in the skull in 2 cases, in the ilium in 2 cases, in the vertebræ in 4 cases, and in the femur (in all cases in the trochanteric region) in 7 cases

In the cases of solitary myeloma which later became generalized, two had Bence-Jones proteinuria before generalization occurred Two patients developed Bence-Jones proteinuria only after spread of the disease Among the patients who retained a solitary myeloma throughout, 2 had Bence-Jones proteinuria The finding of Bence-Jones proteinuria with a solitary lesion supports the diagnosis of myeloma, although this is not usually present in the early stage of the disease

Certain of the cases show radiological and histological peculiarities The radiological appearance in some of the cases was that of a giant cell tumor and in some a malignant invading growth was histologically noted These peculiarities in the roentgenological findings and clinical course must be borne in mind in differentiating giant cell tumors and myelomas

As to treatment, one cannot draw conclusions from the limited number of cases and the varied treatment used It is well known that radiation therapy may control the disease over a certain period of time We have no definite proof that intense treatment will cure the disease even though begun in the early stage before generalization has occurred

We acknowledge with thanks the co-operation of Dr Bowman C Crowell for the use of material in the Bone Registry of the American College of Surgeons

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STUDIES OF GALL-BLADDER FUNCTION

XIII The Composition of the Gall-Bladder Bile and Calculi in Gall-Bladder Disease

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In 1863 Thudicum stated that biliary calculi resulted from a decomposition of the bile the process being akin to putrefaction Since that time we have been presented with the stasis-infection theory of Naunyn, the stasis-hypercholesteremia theory of Aschoff and Bacmeister, the physiochemical theory of Lichtwitz, and a host of others The continued interest in the mechanism of biliary calculous formation is evidence that no one of the many theories already advanced satisfactorily explains the various types of calculi found in biliary tract disease

The frequency of gall-stone disease has been well brought out by Mentzer (6) who reported an incidence of 15 per cent in the adult population of this country Furthermore biliary tract disease is the second most frequent indication for abdominal operations in general surgical practice

We have previously reported (5) that when the gall bladder of man becomes damaged, there occurs a change in the composition of the gall-bladder bile In this paper we are reporting data on the composition of the bile and calculi, when the latter were present, removed at operation from patients exhibiting various stages of gall-bladder disease Although the composition of the gall-bladder bile at the time of operation may not be similar to the composition of the bile at the time calculi were being formed, the study of the bile in a variety of supposedly different pathological states and in the presence of calculi of dissimilar composition is of interest

METHODS

The bile specimens were removed at operation by aspiration of the gall-bladder contents, the patients having had their last meal from 12 to 15 hours previous to operation In the majority of instances the operation was done under spinal anesthesia

The calculi found were imbedded in Wood's alloy When the block became hard it was divided One-half of the stone, imbedded in the alloy was thus kept for permanent record and the other half was recovered by again melting the metal This portion was powdered, dried in the oven at 105 degrees C for 24 hours, and used for analysis Analysis of the stone was made as follows. The dried powder was extracted in a Soxhlet with petroleum ether The extract was evaporated to dryness and the cholesterol determined colorimetrically The residue was extracted with 10 per cent hydrochloric acid Calcium and phosphorus were determined in the neutralized extract by the methods of Clark and Collip and Youngburg and Youngburg, respectively Pigment was extracted from the residue by boiling butyl alcohol and determined by the method of Hooper and Whipple with the modification of Rous and McMaster The material left formed the "undetermined" residue

The methods used for the chemical analyses of the bile have been reported by us in previous papers No bile specimens were used which were contaminated with blood

RESULTS

I Non-calculous cholecystitis In Table I are given the data from 26 patients with non-calculous cholecystitis We realize that this group is not clearly defined and that although the clinical and laboratory examinations prior to operation may strongly indicate the presence of gall-bladder disease, the findings at the time of operation often do not confirm the pre-operative findings Graham and Mackey have recently pointed out also that a diagnosis of chronic cholecystitis from histological sections is not always entirely reliable In Table I we have, therefore, included only data from patients in whom the gross examination at opera-

TABLE I.—COMPOSITION OF BILE IN NON-CALCULOUS CHOLECYSTITIS

Patient	Calcium	Chloride	Bile salt	Cholesterol	Ratio	X ray
	m Eq / L	m Eq / L	mgm / Per cent	mgm / Per cent		
Ne	[illegible]		[illegible]	[illegible]	7	Visualized
Sc		36	[illegible]	[illegible]	4 9	Not visualized
Ch	8	13	[illegible]	[illegible]	6	Not visualized
Sa	24	27	[illegible]			Visualized
Pe	[illegible]	3	[illegible]	[illegible]	[illegible]	Visualized
Li	[illegible]	[illegible]	[illegible]	744	6	Not visualized
Ha	3	32	[illegible]	[illegible]		Visualized
Co	[illegible]	37	[illegible]	333	7	Not visualized
Ar	34	41	[illegible]	176	11 8	Visualized
Bu	[illegible]	42		33		Visualized
De	5	[illegible]	[illegible]			Visualized
Mo	5	44	[illegible]			Visualized
Fly	13	33	[illegible]	273		
Sc		37	[illegible]	[illegible]	9 9	
Ro		[illegible]	[illegible]			Visualized
Ha		44	[illegible]	78	13	
Bl		49	32			Visualized
McK	[illegible]	7	[illegible]	973	17 5	
Ba	8	74	[illegible]	[illegible]	3 4	Not visualized
Ra	[illegible]	32	[illegible]	[illegible]	5	
Gr	13	[illegible]	[illegible]	33	5	Visualized
Du		[illegible]	[illegible]			
Ma	14	[illegible]	[illegible]	[illegible]	7 9	Visualized
Gr	[illegible]	[illegible]		[illegible]		Not visualized
Ma	4	[illegible]	34	4	6 8	Not visualized
Fl	8	18	[illegible]	[illegible]	4 8	

tion suggested cholecystic disease and which diagnosis the histological examination of the tissue later substantiated

The calcium concentrations in this group varied from 4 to 36 milliequivalents per liter with a mean of 16 milliequivalents per liter The chloride concentrations varied from 1 to 118 milliequivalents per liter the mean being 57 milliequivalents per liter The bile salt expressed as sodium cholate varied from 1 to 9 100 milligrams per cent with a mean of 2,813 milligrams per cent. The cholesterol concentrations were equally divergent ranging from 4 to 1 828 milligrams per cent with a mean of 383 In patient No. 8 the data on calcium chloride, and bile salt show that the gall bladder was concentrating practically normally although the gall bladder failed to be visualized on several occasions after the administration of sodium tetraiodophenolphthalein, while in patient No. 6 the gall bladder was visualized even though the evidences of bile concentration, at least as regards calcium and bile salt, were not nearly so good.

Of the 26 specimens 19 had a chloride concentration below 80 milliequivalents per liter while in 4 instances the concentration was below 20 milliequivalents per liter which we believe to be within the normal range. In not a single instance in the entire group however were the chloride, calcium, and bile salt concentrations all within the normal range for gall-bladder bile. The general tendency was for the lower calcium concentrations to be associated with the higher chloride and lower bile salt concentrations. There were, however many exceptions to this general rule.

II Calculous cholecystitis—In Tables II and III are given the data from the specimens obtained from the chronically diseased gall bladders containing calculi. They are divided into two groups depending upon the ability of the gall bladder to be visualized after the administration of sodium tetraiodophenolphthalein In Table IV are given the data obtained from the bile in gall bladders containing stones but in which there was evidence at operation of an acute cholecystitis.

In Group A (chronic calculous cholecystitis —gall bladder visualized) the calcium values varied from 5 to 44 milliequivalents per liter with a mean of 15. The chloride concentrations ranged from 7 to 110 milliequivalents per liter the mean being 61 while the bile salt concentrations varied from 0 to 7,350 milligrams per cent with a mean of 1 560. The cholesterol concentrations ranged from 0 to 1,600 milligrams per cent the mean being 480.

When the gall bladder had not been visualized by the X ray after dye administration (Group B) the calcium concentrations were found to vary from 2 to 25 milliequivalents per liter with a mean of 10, and the chloride concentrations varied from 57 to 140 milliequivalents per liter with a mean of 102 In this group the bile salt concentration ranged

TABLE II—THE COMPOSITION OF BILE AND STONES IN CALCULOUS CHOLECYSTITIS GALL BLADDER VISUALIZED

Patient	Bile					Stone							
	Calcium	Chloride	Bile salt	Cholesterol	Ratio	H_2O	Calcium	PO_4	Pigment	Cholesterol	Residue	Recovery	
	m Eq/l	m Eq/l	mgm per cent	mgm per cent		Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	
He	10	7	1000	[illegible]	12.5	[illegible]	0	0	Trace	96.4	4.2	102.7	Whole stone
Li.	15	[illegible]	[illegible]350	—	—	4.0	1.0	0.1	0.2	86.6	3.2	99.2	Center
						0.4	[illegible]	Trace	0.4	96.8	4.6	105.0	Periphery
Ri	[illegible]	34	[illegible]110	144	[illegible]	11.1	2.1	1.2	3.7	0.5	21.0	59.6	Whole stone
Br	27	38	1[illegible]10	750	16.0	0	1.0	Trace	2.[illegible]	96.0	0.3	100.0	No 2
						4.5	4.9	Trace	0.6	[illegible]9.6	0	0.2	No 1 center
						3.2	2.6	0.3	4.5	8.1	5.9	103.6	No 1 periphery
Fo.	17	40	1000	25[illegible]	3.5	0.0	14.5	2.1	1.7	41.0	10.1	70.3	Center
						0.0	14.0	0.2	1.0	59.6	7.8	83.5	Periphery
Va.	—	41	8[illegible]0	99[illegible]	[illegible]	1.8	[illegible].6	0	0.[illegible]	78.3	6.5	89.6	No 1
						4.9	0	0	1.5	73.9	0.6	[illegible]0.6	No 2 center
						3.0	0.9	0.6	2.0	65.1	1.3	82.5	No 2 periphery
So.	—	48	[illegible]00	—	—	4.4	0	0	Trace	97.7	3.6	100.7	Whole stone
Lit	13	53	83	787	0.1	10.1	3.7	0.3	0.1	80.0	—	91.2	Whole stone
Do	8	35	10[illegible]0	1600	1.1	1.1	4.8	0.2	2.0	8[illegible]6	0.4	96.1	Whole stone
P f	24	59	1.00	320	3.7	0.5	2.1	Trace	0.6	116.0	2.1	1[illegible]1.3	No 1
						0.4	6.1	Trace	0.4	96.0	0	103.1	No 2
Br	14	59	1130	278	4.[illegible]	3.4	3.9	0	Trace	87.3	9.2	103.8	Whole stone
Tr	—	59	Trace	—	—	22.6	0	0	Trace	6[illegible].0	0	80.5	Whole stone
Fo	11	60	1875	377	5.0	1.1	1.8	Trace	Trace	101.8	0	107.7	Whole stone
Sm.	[illegible]3	61	3600	400	9.0	0.2	1.6	0.1	0.5	79.6	0	82.0	Whole stone
Os	14	62	31[illegible]0	368	8.5	1.1	Trace	0	Trace	88.0	0	89.1	Whole stone
It.	8	64	1800	1140	1.5	4.1	0	0	0.5	99.9	Trace	104.0	Whole stone
Ro	6	67	950	97	9.8	[illegible]0	15.7	0	27.2	25.7	—	70.6	Whole stone
Re	12	6[illegible]	0	209	—	4.3	7.3	Trace	0.2	76.9	—	88.7	Whole stone
We	10	68	880	445	5.1	4.0	12.5	0.3	0.9	74.5	4.9	97.1	Whole stone
Sl	6	69	1890	195	9.6	4.3	3.6	Trace	0.8	77.6	0	86.1	Center
						4.5	5.4	Trace	Trace	81.2	0	88.6	Periphery
Ha.	8	81	830	—	—	0.5	1[illegible].0	Trace	1.5	30.5	12.5	50.6	Whole stone
Ba.	12	83	0	339	—	0.9	21.0	0	1.1	70.3	12.8	105.1	Whole stone
Wa.	—	90	9[illegible]0	[illegible]65	1.2	3.9	0	0.4	0.5	88.8	8.3	101.9	Center
						3.8	0	0.1	0.4	109.0	0	113.3	Periphery
Ca	5	93	0	0	—	3.8	28.5	Trace	3.9	58.0	7.0	100.9	Center
						3.1	6.0	0.3	3.8	62.1	7.8	103.3	Periphery
Kr	44	106	—	—	—	8.3	Trace	Trace	0.4	85.0	6.2	99.9	No 1 center
						4.8	5.3	1.3	1.0	70.8	12.1	95.3	Periphery
						4.1	Trace	0	0.3	80.3	27.1	111.8	No 2 center
						0.8	0.8	Trace	0.8	97.0	—	99.4	Periphery
Ma.	16	110	0	—	—	0.3	0	0	Trace	82.6	0.9	83.8	No 1
						3.1	1.9	0	0.1	71.3	24.8	101.2	No 2
Gr	—	—	—	—	—	4.6	Trace	0.1	0.2	98.0	0	102.8	Whole stone
Wi.	—	—	—	—	—	4.5	Trace	Trace	Trace	97.9	0	102.5	Whole stone
Mi	—	—	—	—	—	4.7	0	Trace	0.5	91.5	0	96.6	Center
						4.0	1.2	Trace	Trace	82.7	0	87.9	Periphery

TABLE III.—THE COMPOSITION OF BILE AND STONES IN CALCULOUS CHOLECYSTITIS GALL BLADDER NOT VISUALIZED

Patient	Bile					Stones							
	Calcium	Chloride	Bile acid	Cholesterol	Excess	H_2O	Calcium	PO_4	Pigment	Cholesterol	Remainder	Inorganic	
	m Eq /L	m Eq /L	mgm per cent	mgm per cent		Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	
[illegible]	—	[illegible]	[illegible]	[illegible]	[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Whole stone
[illegible]	[illegible]	[illegible]	[illegible]		[illegible]	[illegible]	[illegible]		Trace	[illegible]	[illegible]	[illegible]	[illegible]
								Trace		[illegible]	Trace	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Trace	Trace	[illegible]	—	[illegible]	Whole stone
[illegible]	[illegible]	[illegible]	[illegible]			[illegible]	[illegible]			[illegible]	[illegible]	[illegible]	[illegible]
						[illegible]	[illegible]		[illegible]	[illegible]		[illegible]	[illegible] center
						[illegible]	[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	Periphery
[illegible]	[illegible]	[illegible]		[illegible]	—	[illegible]		Trace		[illegible]		[illegible]	Center
						[illegible]		Trace		[illegible]	[illegible]	[illegible]	Periphery
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
							[illegible]			[illegible]		[illegible]	[illegible] center
							[illegible]	Trace		[illegible]		[illegible]	Periphery
[illegible]	[illegible]	[illegible]		[illegible]	—	[illegible]	[illegible]			[illegible]	[illegible]	[illegible]	Center
							[illegible]	[illegible]		[illegible]		[illegible]	Periphery
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		[illegible]		[illegible]	[illegible]	—	[illegible]	Center
							[illegible]	[illegible]	[illegible]		[illegible]	—	Periphery
[illegible]	—	[illegible]		—	—	[illegible]	Trace	Trace	Trace	[illegible]		[illegible]	Whole stone
[illegible]	[illegible]	[illegible]			—	[illegible]	[illegible]	Trace	[illegible]	[illegible]		[illegible]	Whole stone
[illegible]		[illegible]		—	—	[illegible]	[illegible]			[illegible]		[illegible]	Center
						[illegible]	[illegible]	Trace		[illegible]	[illegible]	[illegible]	Periphery
[illegible]				[illegible]	—				[illegible]	[illegible]		[illegible]	Center
						[illegible]				[illegible]	[illegible]	[illegible]	Periphery
[illegible]		[illegible]	[illegible]	[illegible]	—	[illegible]		Trace	[illegible]	[illegible]		[illegible]	Center
							[illegible]	Trace	[illegible]		[illegible]	[illegible]	Periphery
[illegible]	—	[illegible]	Trace	—	—	[illegible]	[illegible]	[illegible]	Trace	[illegible]		[illegible]	Center
						[illegible]	[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	Periphery
[illegible]	[illegible]	[illegible]	Trace	[illegible]	—	[illegible]			[illegible]	[illegible]	[illegible]	[illegible]	Whole stone
[illegible]	[illegible]	[illegible]		[illegible]	—					[illegible]		[illegible]	[illegible] center
							[illegible]	Trace		[illegible]	[illegible]	[illegible]	Periphery
								Trace		[illegible]		[illegible]	[illegible]
[illegible]	[illegible]	[illegible]		[illegible]	—		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Whole stone
[illegible]							[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Whole stone
[illegible]								Trace		[illegible]	—	[illegible]	Center
						[illegible]		Trace		[illegible]	—	[illegible]	Periphery
									[illegible]	[illegible]	—	[illegible]	Common duct
[illegible]								Trace	[illegible]	[illegible]		[illegible]	Gall bladder
								[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	
[illegible]						[illegible]	Trace	Trace	Trace	[illegible]		[illegible]	Whole stone
[illegible]						[illegible]	[illegible]	Trace	Trace	[illegible]	[illegible]	[illegible]	Whole stone
[illegible]						[illegible]			[illegible]	[illegible]	[illegible]	[illegible]	Center
[illegible]						[illegible]	[illegible]	Trace	[illegible]	[illegible]		[illegible]	Periphery

TABLE IV —THE COMPOSITION OF BILE AND STONES IN ACUTE CALCULOUS CHOLECYSTITIS

Patient	Bile					Stone							
	Calcium	Chloride	Bile salt	Cholesterol	Ratio	H_2O	Calcium	PO_4	Pigment	Cholesterol	Residue	Recovery	
	m.Eq./L.	m.Eq./L.	mgm. per cent	mgm. per cent		Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	
Sl.		45	1030	6.5	—	0.6	1.4	Trace	1.8	69.5	0.3	82.9	Whole stone
Sp.	12	68	—	—	—	0	33.1	1.9	0	32.1	—	57.[illegible]	Center
						0.4	6.1	2.9	0.3	75.7	3.4	88.8	Middle
						1.[illegible]	11.1	1.1	0	60.9	33.7	109.0	Periphery
Ca.	0	72	4100	—	—	1.0	9.0	0	0.7	72.7	3.0	86.4	Whole stone
La.	7	83	0	118	—	4.[illegible]	5.8	Trace	1.1	89.1	—	99.8	Whole stone
Da	8	86	0	27,	—	4.3	3	Trace	1.2	82.3	—	90.1	Whole stone
Go.	7	91	618	85	7.0	1.7	4.0	2.9	1.0	76.1	2.0	86.8	Whole stone
Br	7	91	0	108	—	3.6	0	Trace	0.2	98.6	0	102.6	Whole stone
We.	7	91	Trace	533	—	4.0	0	0	Trace	80.7	1.8	86.5	Whole stone
Ho.	4	93	83	55	1.5	3.7	3.5	0	0	85.9	—	93.1	Whole stone
Wei	6	100	0	—	—	1.0	Trace	0.4	0	97.8	0.9	102.8	Whole stone
Ar	10	102	930	136	6.8	0.6	0.9	Trace	0	97.0	0	98.6	Whole stone
Gr	[illegible]	105	1080	163	6.6	3.4	0	1.1	3.4	83.0	2.3	94.2	Center
						[illegible].2	19.1	Trace	0.3	42.5	4.3	68.6	Periphery
Ka.	4	113	420	163	0	4.0	3.2	Trace	1.5	68.5	2.9	80.1	Whole stone
Ma.	3	119	0	8	—	5.3	12.7	Trace	1.0	65.0	10.6	91.6	Center
						1.6	3.8	Trace	1.3	61.0	10.6	78.3	Periphery
Sh.	3	1.6	370	122	2.0	5.0	2.9	Trace	1.5	68.5	2.9	80.1	Whole stone
Wi	3	132	0	3	—	0.3	1.2	Trace	1.0	105.0	0.6	—	Whole stone
Ha.	7	133	0	27	—	2.6	0	0	0.6	83.1	4.5	90.8	Center
						6.5	0.5	0	0.1	84.[illegible]	0	91.7	Periphery
Sa.	5	136	31	81	0.4	2.9	8.6	2.1	28.0	8.3	50.6	100.5	Whole stone
Br	6	141	0	Trace	—	4.1	7.5	0.1	0.9	76.7	0	81.8	Whole stone
Gu.	—	—	—	—	—	5.1	0	Trace	Trace	69.7	0	70.3	Whole stone
Sp.	—	—	—	—	—	6.0	2.3	0	0.3	70.6	0.8	80.0	No. 1 center
						8.9	2.8	0	0.6	78.0	1.3	91.6	Periphery
						5.6	0	0	0.4	77.2	1.8	85.0	No. 2 center
						5.4	0	0	0.1	79.8	4.5	90.1	Periphery

from 0 to 3,140 milligrams per cent with a mean of 607, while the cholesterol concentrations varied from 1 to 356 milligrams per cent with a mean of 133

In the acute cases (Table IV) the calcium concentrations varied from 3 to 12 milliequivalents per liter, the mean being 6.5, while the chloride content varied from 45 to 141 milliequivalents per liter with a mean of 101 The bile salt concentration varied from 0 to 4,100 milligrams per cent with a mean of 483, while the cholesterol concentrations were found to vary from 0 to 625 milligrams per cent with a mean of 150

The data in this latter group are without doubt influenced in part by the acute infection present at the time of operation In general, they are not unlike the data obtained from the non-visualized chronic stone cases The mean bile salt value is lower and the mean cholesterol concentration is slightly higher, although the cholesterol concentrations are not as high as one might expect to find in the presence of acute infection

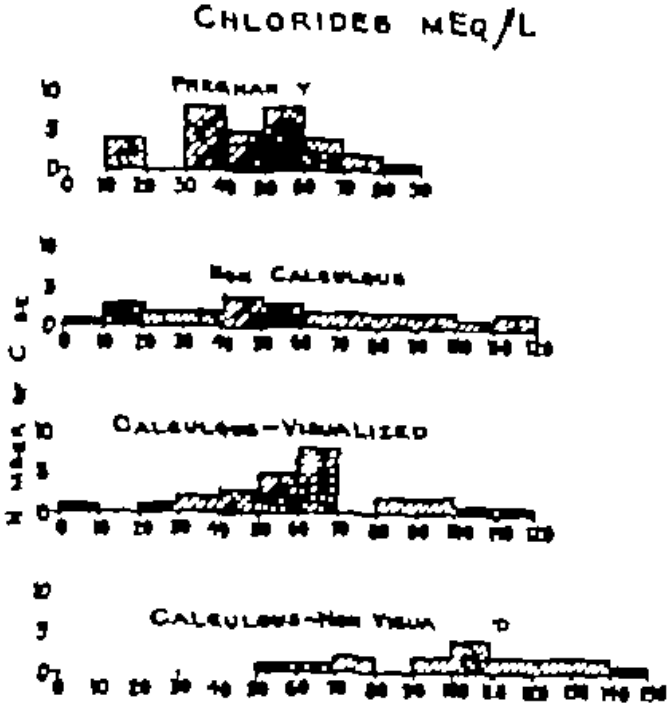

Fig 1 Chlorides

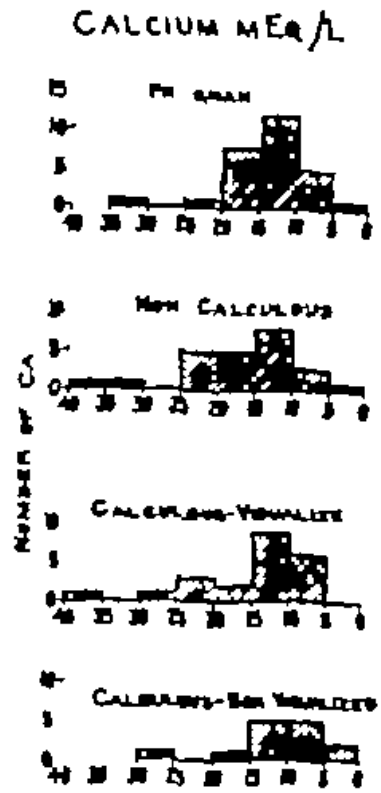

Fig 2 Calcium.

Stones from 73 different gall bladders were subjected to analyses. Roentgen examination of the gall bladder was available in 52 while in 21 instances the patient was not subjected to roentgen studies The analytical data are given in Tables II III IV It can readily be seen that the major portion of each of the stones which we studied consisted of cholesterol. In only a few instances did the calcium content reach 20 per cent of the weight The recoveries in the majority of instances so closely approximate 100 per cent that the amount of undetermined substances present in the calculi was as a rule very small.

One might expect that chemical analysis of the stones would show that the stones which were visualized as opaque shadows would be those with a high calcium content This was not found to be the case. Of the stones visualized as opaque shadows, 19 had a calcium content of less than 10 per cent the remainder having a content of between 10 and 25 per cent. In the entire group of 73 stones from different patients, 61 had a calcium content of less than 10 per cent It is clear therefore, that in the group studied the calcium content of the stones was small

In contrast to the calcium content, the cholesterol content of the stones was high, 67 having a content of more than 40 per cent. Of the 25 stones which were visualized as opaque shadows, after cholecystography 21 had a cholesterol content of over 40 per cent. No pure pigment stones were encountered in this series In 2 instances where it appeared that the calculus might consist chiefly of bile pigments, chemical analysis demonstrated a considerable amount of cholesterol and organic débris and only a small amount of bile pigment.

From this series, it would appear safe to state that positive visualization of the stone after cholecystography gives no indication of its chemical composition. None of the calculi could be considered primary calcium stones, the majority being cholesterol stones with varying amounts of calcium, pigment, and organic débris.

From our data there would appear to be no correlation between the composition of the gall-bladder bile found at operation and the type of stone found in the gall bladder Biles of highly similar composition were found in gall bladders containing practically pure cholesterol stones and in gall bladders containing mixed stones.

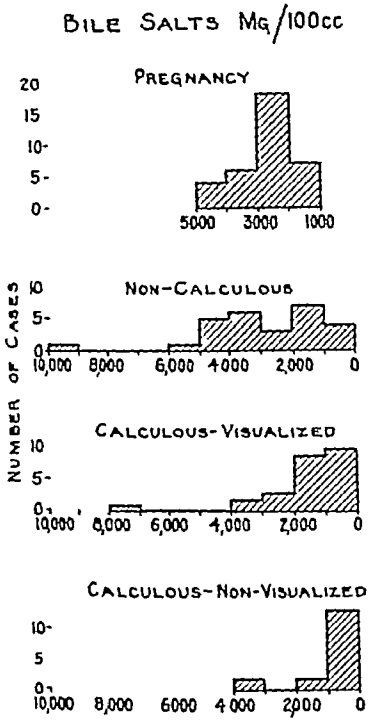

Fig 3 Bile salts

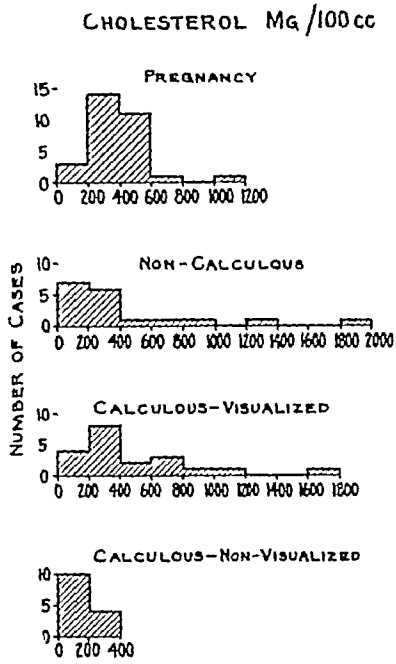

Fig 4 Cholesterol.

EVALUATION OF STUDY

It is now generally agreed that the normal gall bladder changes the composition of the hepatic bile in a consistent manner With the absorption of water from the bile the gall bladder removes chloride and bicarbonate so that the concentrations of these substances in normal gall-bladder bile is only a fraction of their concentrations in the hepatic bile (5, 8) Calcium, bile pigment, bile salt, and cholesterol are concentrated in the gall bladder (4, 9, 10) The evidence at present strongly suggests that normally small amounts of calcium and bile salt are absorbed from the bile while concentration is taking place, and that bile pigment and cholesterol remain quantitatively in the gall bladder during the process of concentration

The data presented in this paper demonstrate that in the presence of cholecystitis the absorbing function of the gall bladder becomes altered

As the gall-bladder wall becomes damaged the chloride concentration of the gall-bladder bile rises This increase in the chloride concentration of the gall-bladder bile may be due to failure of the gall bladder to remove the chloride coming to it in the hepatic bile, or to chloride coming into the bile with any fluid passing into the gall bladder from its wall, or to a combination of these factors

The decrease of the calcium concentration in the specimens from damaged gall bladders may also be the result of several factors The low concentrations frequently encountered in the specimens of gall-bladder bile which we examined may be due to failure of the gall bladder to concentrate the hepatic bile or to the removal of calcium from the solution Evidence which we have previously reported indicated that under the condition of a high carbon dioxide in the gall-bladder bile the calcium in the gall-bladder bile would be partly precipitated as calcium carbonate It is also possible that under the condition of a damaged wall the gall bladder is more permeable to the passage of the calcium ions than normally

The most constant indication of a disturbance of function is a decrease in the bile salt

concentration. With increasing evidence of a disturbance of gall-bladder function there is *nearly uniformly a parallel decrease in the bile* salt concentration.

It was not possible, however to find a parallelism between the conventional pathological diagnosis and the changes in the chemical composition in the gall-bladder bile. In certain instances the bile was removed at a time when the lesion of the gall-bladder wall was progressively becoming more abnormal. In other instances the inflammation which previously had seriously impaired the concentrating function of the gall bladder was subsiding at least to the extent that some concentration of the bile was being accomplished.

No consistent differences were found between the composition of bile in gall bladders containing cholesterol stones and the bile from gall bladders containing stones of the mixed type. There was also no constant direct relationship between pathological classification of the gall bladder and chemical composition of the bile, although it is possible to demonstrate certain gross differences between the biles of the various pathological groups.

Figures 1 2 3 and 4 show the distribution of chloride, calcium bile salts and cholesterol in (a) gall-bladder bile from pregnant women at term, in (b) non-calculous cholecystitis and in (c) and (d) chronic cholecystitis with calculi, the latter group being divided into those gall bladders which were, and were not visualized roentgenographically after the administration of sodium tetraiodophenolphthalein.

It can be seen that as the clinical evidence of increased impairment of function was found the frequency of the chloride concentrations in the higher brackets increased In a similar manner the frequency of very low concentration of calcium and bile salts increased

The bile salt concentrations in the pregnancy group were higher than in any of the other groups except for an occasional specimen. In the non visualized calculous group the greatest number of specimens contained less than 1,000 milligrams per cent of bile salt.

The cholesterol concentrations varied considerably but they were consistently higher in the pregnancy group and lower in the calculous non-visualized group in which a low bile salt concentration was found. In the pregnancy group the bile salt concentration was apparently sufficient to keep a high concentration of cholesterol in solution in bile.

These data indicate certain trends in the chemical composition. We do not feel that they should at this time be treated on a statistical basis, even though when so treated some of the differences between groups appear significant. They nevertheless indicate that in the various stages of cholecystitis, as they are now conventionally given, the degree of impairment of the normal mechanism of concentration varies widely The mere presence of calculi does not always in itself indicate that this mechanism is more pathological than may be encountered in a gall bladder which does not contain stones but which is the site of an inflammatory change.

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UNRECOGNIZED POSTOPERATIVE INFECTION

A Cause of the Syndrome of So Called "Liver Shock"[1]

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NUMEROUS articles dealing with the causes of death following operations upon the gall bladder and the biliary tract are to be found in the surgical literature of the past decade A review of these articles discloses that the reason for individual fatality, in most instances, was recognized readily In not a few cases, however, the cause of death remained obscure Such unexplained deaths, when preceded by a postoperative clinical course which will be described presently, were attributed most commonly to a condition which has been termed "liver shock" ("liver death," "rapid high temperature death") A recent increase in the number of articles devoted specifically to this topic or making reference to it, indicates renewed interest in the subject on the part of physician and surgeon alike Among those who have made contributions may be mentioned — Heyd (13, 14, 15), Cave, Behrend, Stanton, Connell (5, 6), Doran and co-workers Eiss, Shearer, Weiss, Cutler, Schutz, Helwig and Kuhn (20), Guthrie and Robertson, Sharples, Sutton, Boyce (2, 3), and McFetridge (3)

Heyd, who apparently first called attention to "liver shock" following surgical procedures upon the gall bladder and the biliary tract, divides such cases into three groups The latter may be described briefly as follows

Type I In this group are included only cases which are subjected to simple cholecystectomy The patients are neither jaundiced nor acutely ill at the time of operation Shortly after operation there develops without apparent cause, rapidly rising temperature, delirium, and vasomotor collapse This is followed by coma and death, the latter as a rule occurring within 24 to 48 hours

Type II These patients have had a previous cholecystectomy and occasionally a drainage of the common duct Operation is performed for the relief of obstructive jaundice Convalescence is satisfactory for the first few days Then the biliary drainage diminishes in amount, and becomes progressively more watery in character In spite of diminishing jaundice, the patient becomes delirious, then stuporous and finally comatose Exitus occurs in a state resembling cholemia, as noted in patients with unrelieved obstructive jaundice

Type III These patients are not jaundiced They usually are suffering from disease of the common duct or pancreatitis, for which choledochotomy with drainage is performed For the first 24 to 36 hours, convalescence is satisfactory Then the pulse rate becomes accelerated and the patient presents the picture of shock associated with vasomotor collapse, followed by oliguria, then anuria, uremia, fever, and finally coma ending in death

As Cutler has pointed out, Types II and III seem to be in some measure predictable, or at least susceptible of explanation on the basis of prolonged jaundice with probable liver damage on the one hand, and upon diminished renal function on the other Type I however, in view of the excellent general condition of the patient prior to operation, occurs entirely unexpectedly and appears to be entirely unpredictable It is with this type alone, that we are concerned in this communication Accordingly, the term "liver shock," as employed by the author, henceforth shall designate Type I only, unless specified otherwise

The syndrome occurring in Type I "liver shock," as described by several authors (4, 5, 6, 7, 8, 14, 15, 22), may be presented in more detail as follows Within several hours of cholecystectomy, the temperature commences to rise without apparent cause The rise is progressive, and is accompanied by a corresponding increase in pulse and respiratory rates Within 12 to 24 hours, temperature reaches 104 to 107 degrees, and the pulse

[1]From the Surgical Service of Dr Harold Neuhof The Mount Sinai Hospital, New York City Delivered before the Surgical Section of the New York Academy of Medicine January 3 1936

becomes extremely rapid, soft, and often thready The skin becomes cold and clammy blood pressure falls, and cerebral excitation frequently occurs. As the temperature continues to rise, the patient becomes stuporous and finally comatose, the terminal state being one of shock and vasomotor collapse, associated with hyperpyrexia. Death as a rule occurs within 24 to 48 hours following operation, but occasionally may be further delayed by vigorous therapy It has been stated that the more common fatal postoperative complications, such as peritonitis, hemorrhage pneumonia, embolism etc. can be ruled out readily on clinical grounds. Under such circumstances, because of the lack of evidence of any obvious lesion to account for the patient s unusual course following operation the diagnosis of liver shock is commonly made. According to Boyce and McFetridge (3) the only significant finding to be noted at postmortem examination is degeneration (microscopic) of the liver of varying degree. Connell (6) on the other hand stated that he had repeatedly failed to find sufficient liver abnormality at postmortem examination to explain death. Whether hepatic degeneration, when it exists, is the cause of death or is merely the evidence of some profound intoxication is still the subject of debate. Considerable difference of opinion has been expressed also as to the mechanism involved in the production of the syndrome under discussion Some of the theories which have been evolved are based purely on clinical observation others on the results of postmortem examination, and still others on animal experimentation. Since they are not germane to the subject of our discussion they will not be reviewed but those who are interested will find ample material for consideration in the articles listed in the appended bibliography

In connection with our discussion it is significant that in the literature the reported incidence of liver shock following cholecystectomy varies widely the range being from 0 to 34 per cent. Such variation in incidence reported by observers who employed a fairly well standardized technique in operating upon a clearly defined group of patients led us to examine the criteria which were employed in establishing the diagnosis. It was found almost at once that these criteria were far from uniform and that they varied not only with different authors but also with individual cases in series reported by individual authors. Thus, in certain cases, the diagnosis was based entirely on clinical and laboratory data. In others, the clinical diagnosis appeared to be confirmed by incomplete postmortem examination while in still others, it appeared to be confirmed by complete postmortem examination. *In the great majority of instances no postmortem examinations of any type were performed In the comparatively small number of cases in which autopsies were performed few appeared to be adequate.* The author designates as "adequate, only those examinations which included a study of the brain and spinal cord whenever the routine examination of the abdominal and thoracic contents proved negative.

It is realized that often it is difficult to obtain permission to perform postmortem examination. Nevertheless, lacking such examination, the question arises as to whether it is justifiable to accept a diagnosis of "liver shock without reservation. It is to be emphasized that this diagnosis is one of exclusion, and is permissible only after all other complications responsible for hyperpyrexia and early death have been ruled out. It may be claimed that such 'ruling-out is not difficult, and that postmortem confirmation although desirable, is not essential. By way of answer, one has only to recall the desperate condition of the patient following operation, the extremely toxic state the restlessness due to delirium or the lack of co-operation resulting from stupor to realize that the accurate elicitation of physical signs and symptoms of some of the more common postoperative complications often is difficult or impossible. The author now proposes to demonstrate the correctness of this statement. In the first place it will be shown that virulent infection may produce a clinical syndrome which is identical with that of so called "liver shock." Secondly it will be demonstrated that the evidence of such infection may not be detected because the patient may

be so acutely ill as to be incapable either of being examined thoroughly or of co-operating with the examiner in the elicitation of existing physical signs Finally, it will be shown by postmortem studies that patients in whom the clinical diagnosis of "liver shock" was entertained or actually made for apparently justifiable reasons died of other complications

As has been stated previously, it is not our purpose to discuss the various causes of "liver shock," nor to question whether or not such an entity exists It is our object, rather, to point out various pitfalls that are to be avoided in making the diagnosis and to emphasize the fact that serious errors may be committed if care is not exercised to corroborate the clinical diagnosis by adequate postmortem examination The implication, under such circumstances, is that many unconfirmed clinical diagnoses are incorrect and that therefore the incidence of genuine "liver shock" must be considerably less than has been stated by some; unless one includes under the diagnosis of "liver shock," all cases of high temperature and early death after cholecystectomy, the causes of which are not determined

The author became interested in the subject as the result of an experience (Case 1) in which a death which appeared unquestionably to be due to "liver shock," was found at subsequent postmortem examination to have been caused by unrecognized extensive subphrenic suppuration Not only was the latter not detected during life, but its presence was not even suspected In this connection, the following quotation from Stanton is significant "Subdiaphragmatic abscess is very rarely diagnosed clinically On the other hand, it appears to be rather frequently found at autopsy I believe that it is a more frequent complication of gall-bladder operations than the figures would indicate"

As a result of the experience cited, the surgical records of the Mount Sinai Hospital for the years 1928 through 1933 were investigated, for the purpose of subjecting suspected cases of postcholecystectomy "liver shock" to more intensive study During the above period 1,360 cholecystectomies were performed, of which only those that terminated fatally were reviewed Of the fatal cases, a study was made *only of those in which the postoperative course was unexplained on clinical grounds and at the same time corresponded with that of so called "liver shock"* Of these, *we excluded all cases that were not subjected to complete postmortem examination or to examination that was sufficiently complete to explain readily, the cause of death* All patients who were jaundiced or acutely ill at the time of operation were eliminated from consideration, as were those who had been subjected to previous operative procedures on the gall bladder and the biliary tract

The material consists therefore of a series of cases, subjected to simple cholecystectomy with drainage, in which the patients were neither jaundiced nor acutely ill at the time of operation and had not been subjected to other operations upon the gall bladder or the biliary tract Following operation they developed without apparent cause, the classical syndrome of rapidly rising temperature and shock, with early fatal termination, and were subjected subsequently to adequate postmortem study It will be seen that these cases, of which there were 4, correspond to those which Heyd has designated as "liver shock," Type I

CASE REPORTS

CASE 1 M F, a female, 26 years old, was admitted to The Mount Sinai Hospital with a history of recurrent, typical attacks of acute cholecystitis The present attack began 3 days before admission and was characterized at onset by sudden, severe, cramp-like pain in the right upper quadrant, which radiated to the back Pain was accompanied by fever and vomiting At the time of admission, the former had begun to subside

On physical examination, temperature was 102 degrees, pulse, 100, and respiration, 20 White blood cells numbered 13,300 Polymorphonuclear leucocytes were 88 per cent A tender mass was present in the right upper quadrant, but muscular rigidity was absent

The patient was observed for 7 days during which the temperature and pulse rate gradually fell to 99 and 66 degrees, respectively Spontaneous pain disappeared, although slight tenderness and a palpable mass remained X-ray examination, after the oral administration of dye, revealed faint visualization of the gall bladder but no stones

On the afternoon of the eighth day following admission, operation was performed under nitrous oxide gas oxygen ether anesthesia. A distended gall bladder filled with turbid grayish fluid and containing a single mulberry stone impacted in the ampulla, was found. Cholecystectomy with drainage and incidental appendicectomy were performed. Operation was uneventful and the patient was returned to the ward in good condition. During the night her temperature gradually rose, and by morning (16 hours after operation) had reached 104.8 degrees. At that time, pulse was 148 and respirations 36. The abdomen was soft, not tender and not distended. Six hours later (22 hours after operation) temperature was 108.4 degrees, pulse was 180, blood pressure was 60/0, and the patient was comatose and in profound shock. In the meantime, vigorous and continuous antishock therapy had been instituted. Although the temperature could be brought down by means of ice-packs, ice-cold colonic irrigations, and anti-pyretics administered intravenously it would again rise quickly to its former level. After lapsing into coma 24 hours after operation, the patient never regained consciousness, although life was sustained for 48 hours by means of continuous, day and night therapy

Repeated hemoglobin readings of 98 per cent seemed to preclude hemorrhage as the cause of the clinical picture. Diffuse peritonitis was ruled out on clinical grounds, as well as by two negative peritoneal aspirations The day before death, the blood urea-nitrogen was 35 milligrams per cent. Urinary output remained adequate at all times The clinical picture of unexplained rapidly-rising fever rapid pulse and respiratory rates, profound shock, coma, and death in hyperpyrexia, made the diagnosis of "liver shock" appear practically certain. The diagnosis seemed further supported by the absence of evidence of intra-abdominal hemorrhage, peritonitis or pneumonia. The increased blood urea nitrogen, as pointed out by Heyd, appeared to confirm further the diagnosis.

At postmortem examination the essential findings, much to our surprise, were as follows

1 Large serofibrinopurulent subphrenic abscess (right side)

2 Acute serofibrinous pleuritis (supradiaphragmatic) (right side)

3 Acute serofibrinous peritonitis (localized to the operative site) Culture of pus from subphrenic abscess Streptococcus hemolyticus and Staphylococcus aureus

If postmortem examination had not been performed in this case, it would have been justifiable on clinical grounds, to attribute death to "liver shock" Autopsy however demonstrated that virulent intraperitoneal infection was responsible for the lethal outcome. It is important to note that the clinical manifestations of infection were so fulminating that their significance was not appreciated during life.

Case 2. R.N., a female, 40 years of age, was admitted to The Mount Sinai Hospital for the correction of a complete prolapse of the uterus She also gave a history of occasional attacks of right sided abdominal pain, in the upper and lower quadrants, which radiated to the right shoulder blade. There had never been any other associated symptoms. The last attack had occurred 6 weeks previously

On admission, the temperature and pulse rate were normal. A moderately tender globular mass was palpated in the right upper quadrant. X-ray examination after the oral administration of dye, performed on the day following admission, revealed a ring shadow 1 inch in diameter in the region of the gall bladder

The temperature and pulse rate remained normal during an 8 day period of observation, but mild, right upper quadrant pain persisted. Because of the latter it was decided to proceed with cholecystectomy and to postpone operation for the uterine prolapse until a later date.

On the ninth day after admission, cholecystectomy with drainage and incidental appendicectomy were performed. The gall bladder was hydropic and contained a single large stone which was impacted in the region of the ampulla The operative procedure was easily performed, the viscus being removed from below upward.

Following operation, there was a steady rise in temperature and pulse rate At the end of 36 hours, temperature was 106.2 degrees, respiratory rate was 40 pulse was almost imperceptible, and the patient was semi comatose and in shock The abdomen was soft, non-tender, and not distended. There was a free discharge of bile stained fluid along the drain There was no clinical evidence of intraperitoneal or extraperitoneal hemorrhage. The characteristic clinical picture of liver shock was present, and the diagnosis appeared self-evident. At that time, the following significant note was made on the patient's chart, by one of the members of the attending staff "*The patient probably presents one of those cases of postcholecystectomy hyperpyrexia, of undetermined origin which goes on to exitus*" Routine supportive therapy including continuous intravenous infusion of 5 per cent glucose was begun.

Six hours later (42 hours after operation) temperature had reached 107 degrees and the patient appeared moribund On careful check-up physical examination performed at that time, heavy percussion over the lower ribs on the right side appeared to cause pain although this point could not be ascertained accurately because of the patient's sluggish reactions in her semicomatose state On the faint suspicion that suppuration was present, aspiration of the subphrenic space was performed and bile stained pus was immediately encountered. Although

the patient was moribund, so that no anesthesia was necessary, incision and drainage of the subphrenic space was promptly proceeded with, in the faint hope of saving her life A large collection of bile stained, turbid pus was evacuated, but temperature rose to 108 degrees and death occurred about 1 hour later The following essential findings were noted at postmortem examination

1 Defect in the common duct (due to accidental removal of a portion of one wall)

2 Ligated common and right hepatic ducts

3 Leakage from defect in common duct, with bile peritonitis localized to the right lumbar gutter and subphrenic space

4 Status after transdiaphragmatic drainage of right subphrenic abscess

Culture of pus evacuated from the subphrenic space at operation, later yielded the Friedlander bacillus

Aspiration of the subphrenic space was performed, on the basis of a single ill-defined physical sign which was noted when the patient was moribund This sign might easily have been disregarded in view of the patient's condition, and such disregard would have resulted in adherence, before postmortem examination, to the original diagnosis Failure to perform peritoneal aspiration or postmortem examination, probably would have resulted in the case appearing in our records as one of death from "liver shock "

CASE 3 J B , a male, 33 years old, was admitted to The Mount Sinai Hospital with a history of having suffered three mild attacks of right upper quadrant pain, with radiation to both shoulder blades, during the preceding year Each attack lasted 1 or 2 days, and was not accompanied by other symptoms Five days before admission, he suffered an attack which was associated for the first time with jaundice During the day immediately preceding admission, symptoms had begun to subside At the time of admission, the abdomen was soft, relaxed, and not tender Slight icterus was present Temperature, pulse, and respiratory rate were normal At the end of 5 days, all signs and symptoms having disappeared, X-ray films of the gall bladder were taken following the oral administration of dye No stones were demonstrated, but the viscus failed to visualize One week later, during which time the patient was symptomfree, operation was performed

At operation, under general anesthesia, a moderately thick walled gall bladder containing numerous faceted stones was found No stones could be felt in the common duct Typical cholecystectomy, with drainage and incidental appendicectomy, was performed without difficulty On returning to the ward, the patient was in good condition

Twelve hours later, he was in profound shock, with a blood pressure of 40/20, temperature of 105 4 degrees, pulse rate of 140, and respiratory rate of 40 Hemoglobin was 87 per cent, and there was no clinical evidence of either intraperitoneal or external hemorrhage The abdomen was soft and not tender Routine anti-shock therapy, including a continuous intravenous infusion of 5 per cent glucose, was administered Although the blood pressure rose and symptoms of shock abated to some degree, the temperature, pulse, and respiratory rate remained essentially unchanged for 4 days At the end of that time the patient became comatose, evidence of more profound shock re-appeared, temperature rose to 107 degrees, and death occurred

At postmortem examination, the following essential findings were noted

1 Gangrenous bronchitis, with aspiration bronchopneumonia of both lower lobes

2 Intraperitoneal hemorrhage, localized to the right lumbar gutter

3 Large collection of blood, localized between the lower border of the liver and nearby adherent omentum

4 Fat necrosis over the pancreas, omentum, and mesentery

The pathologists considered the cause of death to be the severe pulmonary infection, and intraperitoneal hemorrhage as a contributing factor The rôle of the fat necrosis in contributing to death, was difficult to evaluate Aside from a mild unproductive cough which appeared on the third postoperative day, symptoms of acute respiratory disease sufficient to attract attention, were not present The chest had been examined anteriorly and laterally on several occasions but, in view of the absence of any findings of note, the patient, who was very ill, was not turned to have his chest examined posteriorly With failure to detect sufficient physical findings to explain the clinical syndrome, the diagnosis of "liver shock" would have seemed justified on clinical grounds had postmortem examination not been performed

CASE 4 M W , an obese female, 63 years of age, was admitted to The Mount Sinai Hospital with a history of mild, cramp-like, generalized abdominal pain associated with low grade fever of 6 days' duration Vomiting had occurred only once There had been no previous similar attacks On admission, slight icterus was present Temperature and pulse rate were normal Slight tenderness without spasticity, and a small rounded mass were noted in the right upper quadrant White blood cells numbered 12,000, polymorphonuclear leucocytes, 62 per cent Blood pressure was 134/78

Jaundice disappeared on the day following admission, at which time the Van den Bergh test was

normal. Blood urea nitrogen and cholesterol also were normal. During a 9 day period of observation, the patient was symptom free and pulse and temperature remained normal. On the tenth day operation was performed. Under general anesthesia, a large, thin walled, chronically inflamed gall bladder containing turbid bile and several small calculi, was removed. The common duct was moderately dilated, and contained a single small calculus which was removed. The small opening made in the common duct, was closed by 3 interrupted sutures. Drainage was instituted to the liver bed and to the foramen of Winslow. Because of technical difficulties and time expended in closing a perforation accidentally made in the colon while opening the peritoneal cavity the operative procedure lasted almost 2½ hours.

On her return to the ward, the patient's general condition appeared to be satisfactory. Sixteen hours later temperature was 104.2 degrees, pulse rate 122 and respiratory rate 38. At that time she became quite restless. Four hours later (24 after operation) temperature was 105.4 degrees, pulse rate 144, and respiratory rate 63. The skin was cold and clammy and the patient was irrational and in shock. In spite of vigorous therapy she died one half hour later with hyperpyrexia unchanged, the cause of death being entirely unexplained.

At postmortem examination the following essential findings were noted

1. Severe hemorrhagic pneumonia of the entire right lung.
2. Marked dilatation of the stomach.
3. Coronary arteriosclerosis
4. Adipositas cordis

In the opinion of the pathologists death in this elderly obese patient, was caused primarily by an extensive pneumonia of severe grade, and was contributed to by gastric dilatation. Exitus occurred in approximately 20 hours. The clinical course following operation was unexplained and quite typical of that under discussion. Had it not been for postmortem examination which revealed other causes death could have been attributed to "liver shock."

DISCUSSION

The four cases presented, were selected on the basis of their conformity to the well known clinical syndrome of postcholecystectomy "liver shock." In each instance, no other diagnosis seemed possible. Subsequent postmortem examination revealed, however that death in each case was due to unrecognized infection either intraperitoneal or pulmonary. It may be surprising to many to note that virulent infections at various sites may produce atypical and fulminating manifestations, the causes of which are not only not recognized but not even suspected. These cases constitute the basis of our contention that the common causes of high temperature and early death cannot be excluded with finality in suspected cases of "liver shock," without performing adequate postmortem examination. This does not mean that the usual varieties of postoperative infection cannot be recognized fairly readily for in reviewing the hospital records it was found that not a few deaths due to infection were diagnosed clinically the diagnosis being confirmed subsequently at autopsy.

In these cases the diagnosis was made during life on the basis of symptomatology physical examination laboratory data, and the characteristically irregular postoperative temperature curve despite the fact that in several, death occurred as early as the second or third day after operation. It is of interest to note in passing that in such cases intraperitoneal infection followed operation not only in patients with obviously acute cholecystitis, but also in those in whom the clinical manifestations of cholecystitis had subsided completely or were in the process of subsiding at the time of operation. This is perhaps to be expected in view of the fact that the author in a previous communication (25) demonstrated that active infection of the gall bladder which is usually the source of such postoperative intraperitoneal suppuration, is often present in cases in which clinical manifestations of cholecystitis are absent or minimal at the time of operation.

Connell (5) in 1931 stated that in his experience "liver shock" in abdominal cases followed surgical procedures performed only upon the biliary tract. In other words, he believed that operations upon other intra-abdominal organs were not followed by the occurrence of this complication. Sharples concurred in this opinion. As a result of further observation, however Connell (6) in 1934 modified his original views. At that time he reported the occurrence of six "rapid high temperature deaths" after operations such as hysterectomy oophorectomy appen

dicectomy, and ventral herniopiasty Heuer, Stanton, and Boyce and McFetridge (3) have also noted the occurrence of the syndrome of "liver shock" after operative procedures upon, and traumas to, various organs either within or outside the peritoneal cavity Discussions, similar to those mentioned previously in regard to cases of postcholecystectomy "liver shock," have arisen in regard to these cases also These discussions, since they do not concern us especially, will not be gone into It is important only to point out that in this group the diagnoses recorded in the literature were made in a manner similar to those in the gall-bladder group, few adequate postmortem examinations having been performed to corroborate the clinical diagnoses

To illustrate the importance of performing complete autopsies in suspected cases of "liver shock" in which routine postmortem examination of the abdomen and thorax are negative, the following case is presented

E W, a young man, 19 years old, was admitted to The Mount Sinai Hospital with a typical history of acute appendicitis of 7 hours' duration On admission, temperature was 100 4 degrees, pulse rate 62, and respiratory rate 20 Marked tenderness and moderate spasticity were present in the right lower quadrant The patient also was suffering from a severe acute nasopharyngitis which necessitated operation under spinal anesthesia Nupercaine was employed as the anesthetic agent At operation, an acutely inflamed appendix, distended with mucopus, was removed A small amount of thin, clear, odorless fluid was present in the periappendiceal region Appendicectomy, without drainage, was performed in the routine manner

Following operation, the temperature immediately began to rise and several hours later reached 109 4 degrees At that time, pulse rate was 160 and respiratory rate 48 Mild irrationality, which developed about 5 hours after operation, gave way within another 2 hours to mania that necessitated the administration of large doses of sedatives In spite of vigorous therapy, the rapidly developing shock and hyperpyrexia could not be controlled and death occurred 14 hours after operation (From the foregoing description, it will be seen that the clinical picture following operation, closely paralleled that observed in fulminating cases of postcholecystectomy "liver shock.")

At routine postmortem examination, the essential findings were as follows

1 Acute congestion of all viscera
2 Subendocardial hemorrhages
3 Early hemorrhagic bronchopneumonia of both lungs
4 Persistent thymus
5 Chronic mitral valvular disease

In the opinion of the pathologists, none of these findings was sufficient to explain the postoperative course, and the possibility of acute nupercaine (quinine) intoxication was strongly considered *When the brain and spinal cord were examined, however, the cause of death was found to be an acute diffuse purulent meningoencephalitis*

The foregoing case is of significance for two reasons In the first place, it illustrates in a striking manner the necessity of performing "*complete*" postmortem examinations in all cases of suspected "liver shock," in which investigation of the abdomen and thorax proves negative Failure to examine the brain and spinal cord, after examination of the abdomen and thorax failed to reveal significant findings, would have resulted in an entirely erroneous conception of the cause of death in this case This is especially true in view of the fact that the actual diagnosis was not even suspected during life The second significant point as regards the case, is that it confirms our original contention, namely, that fulminating infection regardless of its site, is capable of producing the syndrome of so called "liver shock "

An important point to be stressed is that in every case in our records, in which the diagnosis of "liver shock" appeared warranted, subsequent postmortem examination proved such diagnosis to be erroneous In view of the fact that cases authenticated by "complete" postmortem examination appear to have been observed by others, however, it is not justifiable to deny the existence of such an entity At the same time it seems only fair to state that one should be unwilling to accept the diagnosis in any case in which the findings are negative, or except for the liver are negative, unless complete postmortem studies have been performed

In view of the observations made by the author, the validity of all diagnoses of "liver shock" which are lacking in such corroboration, is open to question Since most of the cases reported in the literature fall into this category, it appears that in the vast majority of instances they must remain in doubt Therefore it follows that the actual incidence of the condition cannot be stated with

accuracy but it may be assumed to be considerably lower than has been stated by many

It appears significant that the reported incidence of "liver shock as a cause of death after cholecystectomy was highest in those series in which no postmortem examinations were performed and was lowest in those in which such examinations were performed. Thus, Neubof and Anlsea (18) in a contribution entitled "The Cause of Death after Operation, reviewed a series of eight hundred surgical deaths, followed in each instance by postmortem examination. Ninety-one of the eight hundred patients had been operated upon for diseases of the biliary system. In each case the cause of death was demonstrated readily at postmortem examination no instance of "liver shock" being encountered The experience of Heuer with cases of post cholecystectomy "liver shock has been similar for in a recent article he writes as follows "I have never happened to observe a death in cholecystitis without jaundice, as described by Heyd under his Type I in which the autopsy did not reveal conditions sufficient to explain death. Judd and Parker in a paper entitled "Mortality following Operation on the Biliary Tract, Pancreas, and Liver" report a series of 820 cholecystectomies for chronic cholecystitis. In this series there were 12 deaths, postmortem examination being performed in all. None of the deaths was found to be due to "liver shock. In concluding this discussion, a concept expressed by Dr Damon B Pfeiffer and coinciding with that of the author will be quoted In discussing Heyd s (14) paper entitled "Liver Deaths in Surgery of the Gall-Bladder" presented at the annual session of the American Medical Association in 1931 Pfeiffer made the following statement It is well to appreciate the dangers that lurk in operations on individuals with a damaged liver I should deprecate, however the too facile adoption of such terms as "liver shock or "liver death to cover such deaths as appear mysterious and unexplainable I suspect that some are not due to disordered hepatic chemistry but to fulminating infection of a sort not readily demonstrated etc "

CLINICAL APPLICATION

Heretofore, the prognosis of a patient exhibiting the syndrome of "liver shock has been considered to be almost invariably hopeless. Cave expressed this aptly by stating that "It is a startling and helpless situation to follow to its quick termination one of these catastrophes etc. It is our belief as the result of this study that the general attitude in regard to such cases should be modified. This is based on the demonstration that clinical manifestations may not be due to "liver shock" but may be produced by unrecognized fulminating infection. If one can demonstrate such infection to be present and institute adequate therapy it may be possible at times to save life. It must be borne in mind however that an infection which produces such fulminating manifestations is indeed virulent, and demands prompt attention. Therefore it is essential, in view of the seriousness of the situation, to employ without delay every diagnostic measure that will aid in determining the presence of infection, if the latter exists, so that vigorous therapy may follow immediately

Accordingly the following recommendations are made in regard to patients suffering from early postcholecystectomy hyperpyrexia associated with shock of unexplained origin. The abdomen should be examined repeatedly and carefully for evidence of peritoneal irritation Examination should include firm percussion and palpation over the lateral portions of the lower chest and costal margin. Local tenderness thus elicited, is a most valuable presumptive sign of infection of the subphrenic space such infection together with infection of the subhepatic space, constituting the most common suppurative intra-abdominal complications of cholecystectomy Spontaneous pain in the shoulder or tenderness on palpation in the general region of the trapezius ridge, if present, is likewise of great confirmatory significance If no evidence of the existence of intraperitoneal suppuration can thus be found X ray examination should be performed Anteroposterior and lateral films of the chest are taken at the bedside with the patient supported in the sitting position These films must include not only the pul

monary fields but the diaphragms and the subphrenic regions as well Films taken in full inspiration and expiration should be compared, for evidence of diaphragmatic immobility and elevation Such roentgenographic studies will also definitely establish or exclude the presence of pneumonic consolidation, of sufficient extent to account for the clinical course

In the absence of adequate pulmonary or subphrenic findings on X-ray and physical examination, exploratory peritoneal puncture (19) is indicated in an attempt to demonstrate the presence of a suppurative intraperitoneal lesion As illustrated by Case 2, it is especially valuable in those instances in which the patient is already too ill to co-operate satisfactorily in the performance of physical examination or in the elicitation of certain important physical signs The sites of puncture to be preferred, are points lateral to the right rectus muscle at levels somewhat above that of the umbilicus In the event of negative results on aspiration, one should promptly aspirate the subphrenic space in the usual manner If the patient has been operated upon under spinal anesthesia there is still one site to be investigated, if the diagnostic procedures already mentioned have failed to reveal the presence of intraperitoneal or pulmonary infection Since suppurative meningitis without characteristic manifestations may be present (see Case 5), lumbar puncture should be performed Gastric aspiration is recommended in all obese individuals, since unrecognized gastric dilatation in the latter at times may obscure the evidence of a suppurative lesion within the upper abdomen The Levin tube is to be preferred for this purpose, as it can be passed with comparatively little discomfort to the patient and may be left indwelling for continuous drainage if necessary Attention is called, also, to the value of early instituted supportive therapy, including especially the use of the continuous intravenous "drip" (16) as a means of prolonging life Supportive therapy is of added significance, in so far as the longer the patient survives the greater is the probability of arriving at a diagnosis and perhaps of saving life

The actual treatment of any infective lesion which may be discovered, constitutes a general surgical or medical problem depending on its nature, and need not be discussed here Suffice it to say that treatment should be prompt and vigorous, in the hope of occasionally saving the life of a patient whose prognosis otherwise is hopeless

SUMMARY

1 Numerous cases exhibiting a postcholecystectomy syndrome consisting of unexplained rapidly rising temperature, pulse, and respiratory rates, associated with shock and vasomotor collapse, and ending in early death, have been reported in the literature

2 When the existence of postoperative complications such as peritonitis, hemorrhage, pneumonia, embolism, etc are ruled out clinically and no cause of death is apparent, such a syndrome has been attributed commonly to a condition which has been termed "liver shock"

3 The diagnosis of "liver shock" in most of the cases reported in the literature was made clinically, and few adequate postmortem examinations to corroborate the diagnosis appear to have been performed

4 Of a series of 1,360 cholecystectomies reviewed by the author, 4 cases which exhibited the typical postoperative clinical course of so called "liver shock" with unexplained fatal termination, were subjected to adequate postmortem study

5 In each instance, the essential cause of death was found to be unrecognized fulminating intraperitoneal or pulmonary infection, no case of genuine "liver shock" being encountered

CONCLUSIONS

1 In patients, suspected to be suffering from so called "liver shock," it is impossible during life to rule out with certainty the presence of some of the more serious postoperative complications responsible for the clinical manifestations

2 Such complications can be excluded only by adequate postmortem examination

3 The latter therefore constitutes the only means of corroborating the diagnosis of "liver shock"

4 Since the vast majority of diagnoses reported in the literature were made in cases which were not subjected to such examination, the former cannot be accepted with finality and the actual incidence of "liver shock" remains in doubt.

5 The opinion of the author based on a careful study of a small group of cases, is that genuine "liver shock" is much less common than has been assumed generally

6 It appears that in patients suspected to be suffering from "liver shock" unrecognized fulminating infection is the most common cause of the clinical manifestations.

7 All patients exhibiting the syndrome under discussion should be suspected of harboring virulent infection for which early extensive and thorough search should be conducted during life.

8. Infection, if discovered should be dealt with promptly and vigorously in the hope of occasionally saving the life of a patient whose *outlook for recovery otherwise is hopeless.*

The author is indebted to Drs S T Glamer and Arthur Schaffa for permission to report the following case recently observed by them at Another institution.

The patient, A woman of 47 years, was operated upon under the diagnosis of chronic cholecystitis and cholelithiasis. A small thickened gall bladder containing many small stones, was found Cholecystectomy with drainage and incidental appendicectomy was performed, without difficulty under a nitrous oxygen ether anesthesia Following operation the temperature, pulse and respiratory rate began to rise progressively In spite of vigorous therapy temperature rose to 108 degrees, pulse to 180, and death occurred within 48 hours of operation Before death, no satisfactory explanation could be given for the clinical manifestations

At postmortem examination, there was found a serofibrinous peritonitis involving the operative site and the subphrenic and subhepatic spaces On smear the fluid contained numerous gram positive, short chained cocci and a moderate number of large gram positive bacilli On culture, streptococci and Bacillus coli were found the gram positive bacilli failing to grow

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ACCIDENTS OF LOCAL ANESTHESIA

With an Experimental Study of the Toxicity of the Various Anesthetics[1]

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THE rapid increase in the use of local anesthesia has resulted in the appearance of many articles dealing with the various aspects of the subject. Except for a few details, which undoubtedly will be worked out to perfection in the near future, the technique of administration can hardly be expected to be improved As to the anesthetics themselves, many now in use offer perfect results both as to efficiency and harmlessness, but they have one shortcoming, namely, that the duration of the effect of the administration of the drug is too brief It is true that tragic accidents at times do occur following the use of local anesthesia and the patients suffer from serious intoxication or may even die from its use Such untoward results are as unforeseen as a thunderbolt from a clear sky and their causes are entirely unknown Fortunately, in view of the many thousands of operations performed under local anesthesia the world over, these discouraging accidents are exceedingly rare, but they occur often enough to warrant serious study It is a matter of paramount importance, therefore, that reports of such complications be published in full detail and carefully registered, since it is possible to draw practical conclusions only on the basis of an extensive study and from complete statistics In the United States a Committee for the Study of Toxic Effects of Local Anesthetics registers such accidents, and its valuable reports should be of help to all who use local anesthesia In Europe there is as yet no similar committee There are, however, in the European literature several articles which give a thorough and exact account of a large number of cases

A study of these reports convinces me that these cases should be divided into two distinctly separate groups In the first group belong those in which true intoxication results from a relative or absolute overdosage of the anesthetic In such cases typical symptoms have been observed psychic excitation, mental confusion, violent clonic convulsions, partial transient palsies These symptoms may last for a rather long time, but fatal issue is uncommon As for the rest, the symptoms tally with those observed in experimental anesthetic intoxication of animals

In this first group belong 2 cases of Halle Both patients received, by mistake of the pharmacist, a 5 per cent solution of procaine instead of a 0 5 per cent solution Both were given a considerable amount, 300 cubic centimeters, i e , 15 grams, of procaine crystals, which was injected into the soft parts of the face and neck The patients became greatly excited and convulsions were observed, but no lasting damage resulted

The cases of Schuberth also belong in the first group In his first case 125 cubic centimeters of a 0 2 per cent pantocaine solution was poured into the peritoneal cavity, in the other case 175 cubic centimeters of a 0 1 per cent pantocaine solution was injected over a large field into the scalp It is true that the dose did not exceed the safety level in either of the latter cases However, the large, highly resorptive surface of the peritoneum and also the rich vascular supply of the scalp should have been taken into consideration Resorption through the scalp is very rapid, especially if the anesthetic is injected over a large field In the first case cramps were observed for 1 hour, in the second case for 25 minutes

The symptoms in the second group of cases are in sharp contrast with those in the first group In the second group the patient, after having received a comparatively insignificant amount of the anesthetic, suddenly develops a condition closely resembling profound collapse The symptoms are anxiety, dizziness paleness and/or cyanosis, cold and clammy skin, extremely feeble and running pulse, and often loss of consciousness In about one-third of the cases muscular twitchings or even convulsions also are observed In a rather

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great percentage death occurs within a few minutes in spite of all therapeutic measures. Further study of these cases shows the following common factors

1 Except in a few cases, the anesthetic used was cocaine or procaine or both. Cocaine and procaine are the drugs which have been most commonly used for the greatest number of years.

2 The amount of the anesthetic used in the overwhelming majority of cases was very small. In the case reported by E. Mayer a patient aged 20 years, died after 6 cubic centimeter of a 0.5 per cent solution of procaine was given for a tonsillectomy In another case of his the patient died after the injection of 12 cubic centimeters of a similar solution for an operation for hemorrhoids. In one case of Halle—a tonsillectomy—5 cubic centimeters of a 0.5 per cent procaine solution caused death. Schoemaker observed sudden death after the administration of 2 5 cubic centimeters of a 0 5 per cent procaine solution for epigastric hernia. In general the amount of procaine employed ranged from 0.01 to 1 1 grams.

3 The concentration never exceeded the generally accepted limits it amounted, in 90 per cent of all cases, to from 0.5 to 1 per cent. This has been verified in many cases by subsequent chemical examination of the fluid used.

4. The amount of epinephrine used never exceeded the generally accepted dosage. Much heavier dosages are administered to patients suffering from bronchial asthma and other allergic conditions without the slightest inconvenience.

5. Curiously enough, more than the half of all accidents occurred with operations on the neck and two-thirds of these were tonsillectomies. The others were chiefly splanchnic spinal and sacral anesthesias.

6. In a relatively great percentage of cases necropsy showed persistent thymus gland or severe myocardial damage There were, however many entirely negative findings

What is the cause of these unexpected and unforeseen tragedies? Overdosage intoxication in the strict sense of the word can be ruled out, the dosage employed being but an insignificant fraction of the normally tolerated dose. As to accidental intravenous injection, there is no doubt that the passing of a greater amount of anesthetic into a vein may cause serious intoxication or even immediate death Therefore, de Takats recommends great caution in infiltrating highly vascular regions (varicosities, hemorrhoids, deep regions of the neck) In the cases in question, however such small doses have been used that they could not possibly have caused intoxication, even if the full amount had directly entered a vein. Hackenbruch himself says that a few cubic centimeters of anesthetic injected into a vein does not cause any harm. Moreover it is well known that the intravenous lethal dose of anesthetics belonging to the aminobenzoylic ester group (procaine, tutocaine, pantocaine) amounts to one tenth of the subcutaneous lethal dose. It is evident that much greater doses are tolerable intravenously than the doses in question. Epinephrine intoxication may be considered, its symptoms being to a certain extent similar yet not identical. This question has not received sufficient study as yet. As to the possibility of hypersensitiveness —idiosyncrasy some allergy-like condition— it must be admitted that some patients are known to be hypersensitive to local anesthetics In a number of accidents reported the symptoms, too were suggestive of anaphylactic reaction. However this point has not as yet been sufficiently investigated. Systematic skin sensitivity tests were not made Very interesting is Seeger's case of apparently acquired hypersensitiveness The patient died within a few minutes after the administration of a small quantity of the same local anesthetic which at the occasion of a previous operation was well tolerated in a much heavier dosage. If we accept the theory of hypersensitivity the case mentioned is an example of sensitization by previous exposure, similar to acquired protein allergy

In an attempt to explain the accidents of local anesthesia Seeger takes as a starting point the fact that most fatalities occur with operations on the neck. He believes that this is due to anatomical causes On the neck within a narrow space there are crowded together organs of immediate vital importance —vagus nerve, sympathetic ganglia, the

carotid sinus—which can be damaged by the anesthetic in different ways First, the anesthetic may anesthetize or paralyze them by direct diffusion and in this way cause serious disturbances in the organs supplied The great irritability of the denervated heart, e g, is well known Second, pressure produced by the injected solution or the result of a hematoma caused by the inadvertent puncture of a vessel in this highly sensitive region may cause sudden catastrophe In the case of Wiemann there was found, at the site of the injection, a hematoma which compressed the vagus nerve and the upper cervical ganglion Injury to the vertebral or the carotid artery is another possibility Should the fluid be injected inadvertently into an artery, the brain may become flooded with a concentrated anesthetic solution Moreover, in forensic medicine many cases are recorded of immediate death following blows and other injuries to the neck Accidents after local anesthesia in other regions cannot be satisfactorily explained on the basis of these deliberations, however Seeger believes that in general these accidents are caused by some reflex inhibition, the result of a mere physical traumatism That psychic disturbances, too, are liable to play an important part is shown by one case of Halle—the patient collapsed just before the starting of the anesthesia and went into serious shock If this had happened after the anesthetic had been administered, there would have been not the slightest doubt that the collapse was caused by the anesthesia

From the facts mentioned it does not seem justifiable to attribute the accidents belonging in the second group to intoxication, they ought to be regarded rather as instances of a kind of acute shock As to the mechanism of the latter, let us state that it is not well understood Allergy-like hypersensitiveness probably plays a rôle in at least some of the cases

The pathology of those mild intoxications, the symptomatology of which consists of transitory anxiety, palpitation, and sweating, is also unexplained It seems to me that they are due to a specific procaine effect. At any rate, since we discontinued the use of procaine at the Third Surgical Unit of the University of Budapest and began to use, first tutocaine, later nupercaine, and at present pantocaine, we have not observed a single case of such untoward result in a series of more than 15,000 major operations

Therefore with our present knowledge we have not much hope meanwhile of becoming able to prevent or to obviate fatalities belonging in the second group, except perhaps by the use of immediate barbital therapy, the results of which seem to be encouraging True intoxications belonging in the first group, however, can and should be prevented The more extensive use and perfected technique of local anesthesia has resulted in its use in the performance of operations of longer duration and greater extent The performance of these extensive operations often necessitates the use of such large amounts of anesthetic solution that the problem of intoxication due to local anesthetics will probably soon come into the foreground of interest Therefore we have found it worth while to study by animal experiments several factors regarding dosage which may influence our knowledge as to the toxicity of local anesthetics We investigated the following three questions What is the influence of local anesthetics on toxic effects in relation to (1) concentration of the solution employed, (2) the site of subcutaneous injection, and (3) the protracted fractional administration of the anesthetic.

The literature on these three questions is rather scanty We could not find a single paper dealing with a systematic study of the problem, we found only parenthetical remarks concerning this topic According to Haertel the lethal dose administered in a given concentration will not cause death if it is not injected at once but fractionally over a short period of time, a dose lethal in a given concentration will not be lethal if administered in a more diluted solution, data as to the lethal dose of an anesthetic are to be depended upon only if they contain three items amount, concentration, and method of administration Haertel does not mention the rôle of the site of injection Ádám, on the basis of his experiences with a vast surgical material, has come to the conclusion that the toxicity of a local anesthetic is decreased by the use of highly diluted solutions, by injecting them far from the

central nervous system and by the fractional administration of the amount required on the other hand he believes that high concentrations of the solution injection near the central nervous system, and the sudden flooding of the organism with great doses increases the toxic effects. Pouchet injected 40 milligrams of cocaine dissolved in 1 cubic centimeter of water into the peritoneal cavity of a guinea pig and it died another guinea pig received 100 milligrams dissolved in 15 cubic centimeters of water and it survived.

According to Zunz the toxicity of procaine depends on the concentration of a 1 per cent solution not more than 1.25 grams, of a 2 per cent solution not more than 0.75 gram should be employed It is advisable to use a 0.5 per cent solution *Toxikologie* by Starkenstein, Rost, and Pohl mentions only that concentrated solutions are quickly resorbed whereas diluted solutions are bound locally In the experiment of Braun, a rabbit suffered severe intoxication from 0.005 gram of cocaine in a 10 per cent solution injected into the ear vein whereas it tolerated four times the dose mentioned if injected in a 0 1 per cent solution. He does not mention the speed of the injection which in our opinion probably played the major part. The data mentioned seem to show that concentration has a significant influence on toxicity On the contrary according to Martin the lethal dose of procaine for the dog is 300 milligrams per kilogram of body weight, a 10 per cent solution being used. This exactly equals the lethal dose if a 1 to 2 per cent solution is used. Veterinary surgeons use chloral hydrate extensively for intravenous injection, in 5 to 20 per cent solutions. The efficient dose is independent of the concentration (Marcenac, Welscher) There is no doubt that fractional administration greatly reduces toxicity According to Schulemann a quadruple lethal dose of tutocaine may be safely injected into the ear vein of a rabbit if it is administered at a slow rate.

In our experiments we studied four local anesthetics procaine tutocaine, nupercaine, and pantocaine.

Concerning procaine it should be mentioned that both non-proprietary procaine and original novocain of the German firm I. G Farbenindustrie have been assayed, the two being of identical chemical formula We found no difference whatever in their action Of tutocaine we used the original 0 5 gram tablets of the I. G. Farbenindustrie, labelled T III. Concerning pantocaine we tried both the 0.1 gram tablets and pantocaine crystals. We did this because on checking the weight of the tablets we found that their average weight was 0 14 gram. In replying to our question the firm stated that this excess of weight was due to inert binding substance. This statement has been proved to be correct in our experiments. Nupercaine was used in crystalline form Concentrated solutions of the latter (1 to 2 per cent) irrespective of whether prepared with physiologic salt solution or with distilled water are liable to show heavy turbidity on standing for a few minutes and quite soon a crystalline precipitate forms. We do not know the cause of this phenomenon—perhaps the presence of traces of alkali—but at all events we injected the solutions before they had time to become turbid. As for the rest, all solutions have been freshly prepared with a 0 8 per cent solution of sodium chloride. No addition of epinephrine was used because it seemed to us undesirable to be obliged to take into account the toxic action of another by no means indifferent substance. On the other hand, epinephrine retards the rate resorption in an incalculable measure

We started our experiments by determining the minimal lethal dose of the four compounds mentioned. Though these data are to be found in the literature, they are not entirely uniform therefore it seemed to us expedient to determine them once more. These introductory experiments have been performed with solutions of a standard strength (2 per cent) of all the anesthetics to be assayed and only after this were solutions of different concentrations tried. The injections were made into the subcutaneous tissue of the lower abdomen or the inguinal region respectively at one site, forming a circumscribed deposit. The same animal was not used twice within a period of at least 5 days. Each dose was run with 5 animals. The dose which caused the death of at least 3 animals in 5 used was arbitrarily accepted as the minimal lethal dose We noted not only the fact of death, but also the time which elapsed between the injection and death. In the beginning we used white rats, body weight from 110 to 180 grams. It soon became evident, however that this species is so insensitive, so tolerant to local anesthetics that the introduction of the lethal dose in more diluted solutions would have

been impossible on account of the enormous quantity of fluid necessitated When 2 per cent solutions were used we found the following lethal doses

Procaine 2400 milligrams or 120 cubic centimeters per kilogram body weight
Tutocaine 700 milligrams or 35 cubic centimeters per kilogram body weight
Pantocaine 80 milligrams or 4 cubic centimeters per kilogram body weight
Nupercaine 70 milligrams or 3 5 cubic centimeters per kilogram body weight

Consequently 240 cubic centimeters of a 1 per cent procaine solution or 350 cubic centimeters of a 0 2 per cent tutocaine solution per kilogram of body weight would have been the approximate lethal dose This amount of fluid would have been so heavy a burden to the circulation, if injected parenterally, that it would have made valueless the results of the experiments Therefore, we later took guinea pigs because this species is much more sensitive to local anesthetics The course of the intoxication is quite similar in both species It will be described as it is shown in the guinea pig, mention being made also of the differences observed The body weights of the guinea pigs employed ranged from 165 to 740 grams We did not observe any difference in sensitivity as related to on body weight

The symptoms of intoxication from procaine, tutocaine, and pantocaine are quite similar Depending on the dose, after a latency period of from 4 to 20 minutes the animals will begin to tremble and to stagger, and there is a slow nodding movement of their heads At the same time they will drag their hind extremities After 1 to 2 minutes the animals, apparently lame, will turn on their sides and lie motionless After another few minutes violent convulsions will start The head is spastically bent backward, there is an opisthotonos-like stretching of the entire body The extremities perform quick, jerky movements, which, on the whole, seem rather coordinated and resemble running At times the spasms subside only to start anew after a few seconds Often curious twisting, spiral movements of the head are observed The convulsions often are violent enough literally to throw the animals from their baskets Later, the convulsions gradually subside and paralytic symptoms become dominant The animals will lie motionless, with respiration as the only sign of life Later the rate of respiration rapidly decreases and it becomes stridulous, possibly due to spasm of the glottis This condition lasts for a variable length of time In general the animals die within 20 minutes, or there is a reverse succession of the symptoms mentioned with ultimate complete recovery In about 90 per cent of the cases, the entire course of the intoxication is about 1½ hours or less, whether the animal dies or recovers However, a few instances of death occurred after more than 3 hours

Nupercaine intoxication shows a certain departure from the type described The first symptom to be observed is violent psychomotor excitation The animals leap about, snap at all objects within their reach, nibble in an excited way, yell in a curious agitation Very soon, however, they become paralyzed and later go into convulsions The further course of intoxication is very similar to that observed with the aminobenzoylic esters, with the only exception that on recovery there is again a stage of motor excitation In rats, all anesthetics caused identical reactions, quite similar to procaine intoxication of the guinea pig, the convulsions, however, being less violent

The experimental data reported in Table I concern guinea pigs

INFLUENCE OF SITE OF INJECTION ON THE TOXICITY OF LOCAL ANESTHETICS

In these experiments we employed a 2 per cent solution of pantocaine, the minimal lethal dose of which has been found in our previous experiments to be 1 0 cubic centimeter per kilogram body weight if injected into the subcutis of the lower abdomen One-third of this amount—0 33 cubic centimeter per kilogram—has been injected subcutaneously into the submandibular region of 5 guinea pigs No animal died, we did not even observe a single case of somewhat serious intoxication Therefore, another 5 guinea pigs were similarly injected with twice this amount—0 66 cubic centimeter per kilogram One of these animals died after 70 minutes,

TABLE I.—INFLUENCE OF DEGREE OF DILUTION ON THE TOXICITY OF LOCAL ANESTHETICS

1. PROCAINE

2. TUTOCAINE

3. PANTOCAINE

4. NUPERCAINE

Explanation of signs: + dead, □ survival, C convulsions, CC vomiting, P paralysis, E psychomotor excitation. The first column of each section shows the weight of the animal in grams. On second line shows the amount of solution injected in cubic centimeters.

0 025 gm = 1 25 c.cm per kgm

550	0,69	8 minutes later	C	+	after 80 minutes
500	0 63	6 minutes later	C	+	after 44 minutes
340	0 55	6 minutes later	C	+	after 28 minutes
370	0,40	11 minutes later	C	+	after 56 minutes
4 0	0 53	7 minutes later	C	□	

0 5 per cent solution

0 015 gm = 3 c cm per kgm

700	2,1	5 minutes later staggering		□	
470	1,3	14 minutes later staggering	F	□	
5,0	1 ,	ϕ		□	
650	1 05	6 minutes later	E CC	+	
630	1 6	ϕ		□	

0 02 gm = 4 c.cm per kgm

590	2 36	6 minutes later staggering	E C	+	after 46 minutes
520	2 1	8 minutes later staggering	CC	+	after 40 minutes
480	1 9	14 minutes later staggering	CC	□	
380	1,5	17 minutes later	CC	□	
610	2 6	minutes later	F,C	+	after 36 minutes

0 1 per cent solution

0 015 gm = 15 c.cm per kgm

420	6,3	0 minutes later staggering		□	
500	7 5	4 minutes later staggering	F C	□	
4 0	7 1	16 minutes later staggering			
500	7 5	ϕ		□	
560	8,4	18 minutes later	CC	+	after 70 minutes

0 020 gm = 20 c cm per kgm

520	10,4	12 minutes later	F C	+	after 36 minutes
530	10,6	10 minutes later	E,C	+	after 40 minutes
710	14,2	14 minutes later	E,C	□	
560	11 2	1 minutes later	F C	+	after 44 minutes
400	8 0	18 minutes later	E,C	□	

the 4 others showed mild spastic and paralytic symptoms Since it has been unequivocally demonstrated by these few experiments that the site of injection does not noticeably influence the toxic action, we discontinued our investigations in this direction

INFLUENCE OF PROTRACTED FRACTIONAL ADMINISTRATION ON THE TOXICITY OF LOCAL ANESTHETICS

In these investigations we employed a 0 1 per cent pantocaine solution, the minimal lethal dose of which was found in our previous experiments to be 25 cubic centimeters per kilogram of body weight We took 7 guinea pigs, weighing from 480 to 710 grams They were injected each with 5 cubic centimeters of the solution mentioned, every 20 minutes The experiment was continued for 2½ hours, during which time each guinea pig received 9 injections, totalling 45 cubic centimeters This is four times the lethal dose of the smallest animal and almost three times the lethal dose of the heaviest animal In spite of this only 3 animals showed mild symptoms of intoxication — muscular hypotonia, abortive cramps—the others did not seem ill at all One hour and a half after the completion of the experiment all animals were quite alert

RECAPITULATION

A survey of the tables shows the following results

1 The toxicity of the anesthetic compounds assayed does not completely tally with data of the literature We do not speak of the surprisingly high lethal doses observed with white rats, as no corresponding data in the literature are available As to guinea pigs the generally accepted lethal doses on subcutaneous injection are procaine, 400, tutocaine, 200, pantocaine, 30 to 40, and nupercaine 10 milligrams per kilogram of body weight Concerning procaine and tutocaine, our experiments confirm these data, whereas we found pantocaine more toxic and nupercaine less toxic than is generally accepted The lethal dose of both pantocaine and nupercaine has been found to be 20 to 25 milligrams per kilogram of body weight According to the hitherto accepted data, the absolute toxicities of procaine, tutocaine, pantocaine, and nupercaine are as 1 2 15 40, whereas their therapeutic indexes are, considering that the anesthetic power of a 1 per cent procaine, a 0 2 per cent tutocaine and a 0 1 per cent either pantocaine or nupercaine solution is equal, as 1 0 4 1 5 4 (Here the term therapeutic index means the relation of the efficient concentration to the minimal lethal dose, procaine being taken as the unit) According to our results the relation of the absolute toxicities of the compounds mentioned is as 1 2 5 22 22, whereas that of their therapeutic indexes is as 1 0 5 2 2 2 2 Consequently, as to toxicity, tutocaine is to be considered the most suitable local anesthetic Then follows procaine and the highest toxicity is exhibited by both pantocaine and nupercaine Of course, only the lethal doses have been used as a basis of comparison and not the other advantages or drawbacks

2 The degree of dilution apparently does not materially affect toxicity, at least not in animal experiments The greatest difference in toxicity observed with solutions of different concentration of the same anesthetic—5 and 0 5 per cent solution, respectively, of tutocaine—did not exceed 30 per cent This is almost within the limits of observational faults and may be practically neglected At

first glance this result is *somewhat surprising* as it could be expected that more concentrated solutions, because of their *quicker* resorption will show a higher toxicity On more thorough consideration, however of the factors involved in and influencing the toxicity of a given agent, it becomes evident that their different concentrations may yield widely divergent results. First, it is rather questionable whether the resorption of a concentrated anesthetic solution is really markedly quicker than that of a more diluted one. It should be borne in mind that even the most concentrated anesthetic solutions in use are highly hypotonic, as far as the anesthetic compound itself is concerned The molecular size of tutocaine for example, is 286 therefore an isotonic solution would have the strength of almost 5 per cent Our routine solutions are much weaker The relatively quicker diffusion of a small volume of a more concentrated solution may also become counterbalanced by the larger surface of a greater quantity of the more diluted solution The importance of the size of the resorptive surface need not be stressed It is exceedingly difficult to perform exact experiments in this respect In the course of our investigations we injected 2 guinea pigs with half the lethal dose of a 0 5 per cent tutocaine solution into the subcutis of the abdomen, over as large an area as possible Both animals died within 45 minutes. Besides this, the concentration in the blood of any given poison is influenced by the proportion between the rates of resorption and of detoxification or excretion, respectively Local anesthetics are quickly detoxicated and neutralized by the organism A rabbit for example is able to neutralize 3 milligrams of procaine or 0 15 milligram of pantocaine each minute per kilogram of body weight (H. Schmidt) In this way the full lethal dose is made harmless in about 2 hours With so quick a neutralization it seems to be open to doubt whether a moderate acceleration of resorption will constitute an actual danger Moreover the toxic action of any agent does not exclusively depend on its concentration in the blood Of course there are poisons the toxic action of which is directly proportional to their concentration in the blood—most of the narcotics—with other poisons, however it depends on the product of concentration and *duration* of action This means that a lower concentration if it acts for a sufficient length of time may produce the same effect as a higher concentration acting for a shorter time (Starkenstein-Rost Pohl) This phenomenon is caused by the fact that it takes a certain length of time for the cells to store an efficient amount of poison from the surrounding fluids (elective fixation storage, cumulation) In this way a more diluted solution if it is being resorbed over a longer period of time may under certain circumstances, prove even more harmful Moreover a cell showing greater avidity for a certain poison is not necessarily the more sensitive one It is even possible that by increasing the concentration such cells will be compelled to take up greater amounts of the poison—cells of liver muscle, kidneys—which are less susceptible to injury by it and in this way the highly sensitive nerve cells will actually be spared It need not be emphasized that this is possible only within certain limits which are determined by a favorable or unfavorable relation between the rates of resorption detoxication, and excretion cumulation and many other factors, a part of which are meanwhile beyond the range of being understood. As a matter of fact, in animal experiments the constellation of these factors is such that the influence of concentration upon toxicity cannot be demonstrated As to human beings, we do not wish at this time to draw positive inferences

3 That the site of the subcutaneous injection is not a main factor is not surprising if resorption takes place exclusively into blood channels, although on the neck resorption is probably quicker because of its abundant blood supply If resorption were to take place by way of lymphatics too, resorption would be quicker from sites connected by a short route with the thoracic duct At any rate the ultimate differences are so slight that they are entirely overcome by the levelling activity of the organism Here we do not deal with the danger of direct diffusion into the central nervous system if the anesthetic is injected too near to the spine, as this is not a problem of toxic action in the pharmacological sense of

the word The curious frequency of fatalities following operations on the neck done with local anesthesia has been discussed already in the early part of this paper

4 Protracted fractional administration greatly reduces the toxic action of local anesthetics as could be foreseen from data gleaned from the literature and from knowledge concerning the pharmacology of the compounds in question

As stated, we do not maintain that our results positively apply to human beings The administration of small doses even of concentrated solutions if necessary, is probably safe If however, large quantities are to be used the diluted solutions are advisable, since among other dangers that of overdosage is thus minimized Moreover it is objectionable to charge the organism with a heavier load of poison than is strictly necessary however mild this poison may be It seems to be expedient, too, if a considerable amount of anesthetic solution is required not to administer it at once, but rather in fractional dosages

SUMMARY

1 Accidents of local anesthesia are to be divided into two groups (a) true intoxication resulting from overdosage and (b) acute shock, the pathological mechanism of which is not well understood

2 In animal experiments variation of the degree of dilution and of the site of subcutaneous injection did not noticeably influence the toxic action of local anesthetics, whereas fractional administration of a total of three to four times the minimal lethal dose over a period of 2½ hours was tolerated by the animals without any serious untoward effect

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CLINICAL SURGERY

FROM THE DEPARTMENT OF SURGERY LOUISIANA STATE UNIVERSITY

JEJUNOSTOMY AS A PALLIATIVE PROCEDURE IN INOPERABLE OBSTRUCTIVE CARCINOMA OF THE STOMACH

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JEJUNOSTOMY which is the creation of an artificial opening in the upper part of the jejunum for the introduction of nourishment, is a procedure which is occasionally useful in inoperable obstructive carcinoma of the stomach It is a short and simple operation which can be done under any type of anesthesia, though the writer s preference is for *nitrous oxide and oxygen* or ethylene anesthesia The decision as to the agent to be employed depends chiefly upon the patient s condition and the surgeon s own desires

The operation is performed in the following steps (1) incision of the abdomen (2) exploration of the abdomen, (3) identification and exteriorization of the jejunum, (4) definition of the groove or channel in which the jejunostomy tube is to lie, (5) insertion and infolding of the jejunostomy tube, (6) closure of the abdominal wall

1 The abdomen is opened through a left paramedian incision, about 6 inches long, the lower limit of which is on a level with the umbilicus A median incision may be used, but an incision slightly more to the left gives a better exposure of the jejunum, which occupies the left hypogastrium, and permits a more satisfactory exploration of the abdominal contents.

2 A careful exploration of the entire abdomen should not be omitted in any case in which the patient's condition warrants the additional time, even though all the clinical and laboratory evidence should indicate that no procedure other than jejunostomy is possible. Jejunostomy as we shall point out later is frankly a last resort, and *while it is definitely indicated in a small number of* cases, it should never be done until a careful exploration has made it clear that no other procedure is feasible

Fig Jejunum held out of ound by intestinal clamps (Modified from Buchbaum)

3 *The upper 12 inches of the jejunum is now* sought for and identified This portion lies just distal to the duodenojejunal junction and is easily identified by its relation to this landmark and to *the ligament of Treitz, as well as by its position in* relation to the second lumbar vertebra, to the left of which it lies. As soon as the bowel is brought up into the wound, the root of the mesentery is palpated, according to the method of *Monks*, to determine that there is no twist in the mesentery This precaution is exceedingly important if the bowel should be twisted, and that fact should not be discovered, the jejunostomy tube would be inserted in the wrong direction and feeding would be impossible Following this investigation, and the untwisting of the bowel if that should prove necessary the portion of the jejunum in which the operation is to be done is held out of the wound (Fig 1) by an intestinal clamp preferably rubber covered, with a soft spring, which is so applied as to extend well beyond the operative field The bowel is then surrounded by gauze packs which have been dipped in warm saline solution

4 The groove in which the jejunostomy tube is to lie is indicated on the antimesenteric *wall of* the gut by the application of Allis forceps, or better by long traction sutures of silk (Fig 2) Sutures do less damage to the bowel wall, and are useful later in fastening the jejunostomy tube in position. The groove in which the tube is to lie should be at least 4 inches long the longer it is, the more securely is the tube held in place and the less likely is leakage to occur

5 A stab wound half an inch long is made into the intestinal lumen 1 inch above the lower trac

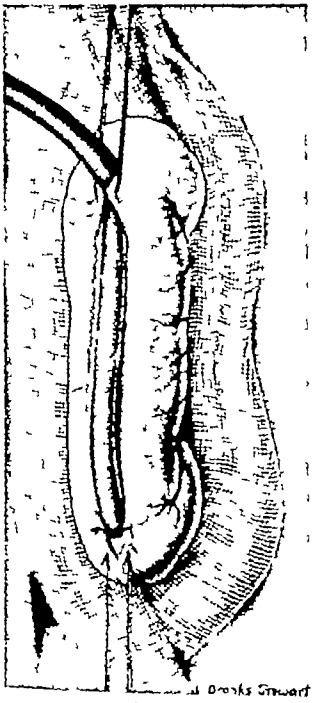

Fig 2

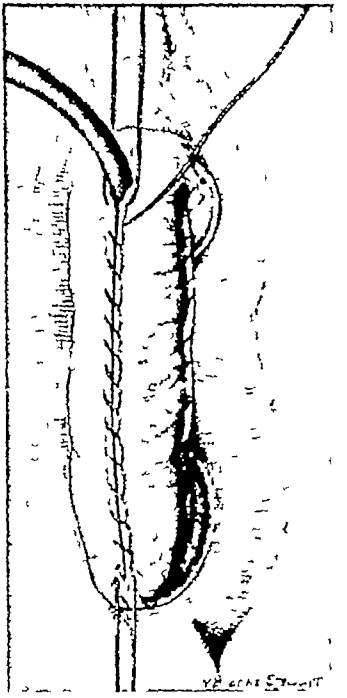

Fig 3

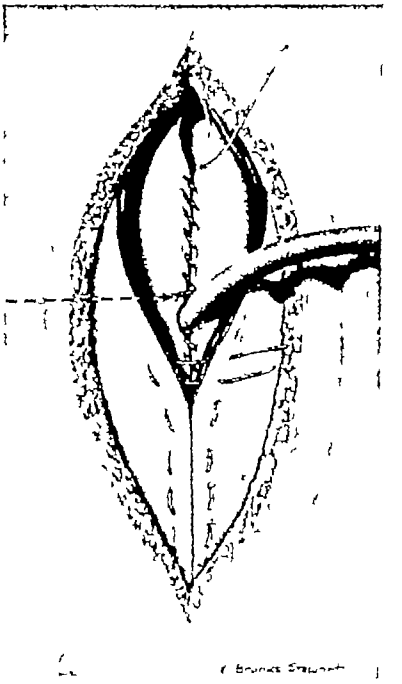

Fig 4

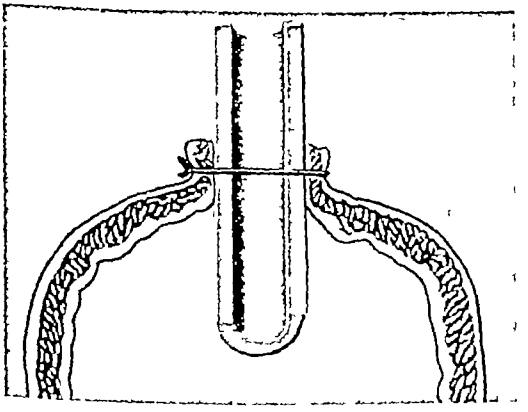

Fig 2a

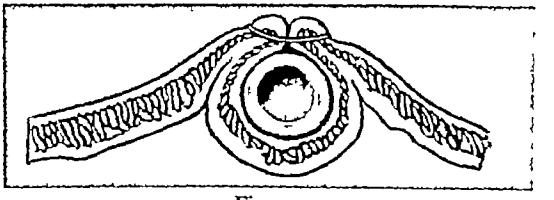

Fig 3a

Fig 2 Tube lying on wall of jejunum, in groove outlined by upper and lower traction sutures held on tension, after it has been inserted into lumen of bowel and fastened by transfixion suture. a, Cross section of jejunum, showing tube inserted into lumen and fastened in place by transfixion suture

Fig 3 Tube buried in groove formed by fold of jejunal wall Burial accomplished by continuous Lembert sutures a Cross section showing the tube buried in the wall of the jejunum

Fig 4 Closure of peritoneum and fascia after fixation of jejunum to peritoneum by upper traction suture (indicated by arrow) Note special mattress sutures of silk to close aponeurosis of rectus muscle

tion suture The opening must be sufficiently large to permit the entrance of a No 16 French catheter, but not large enough to permit leakage about it The tip of the catheter is inserted into the stab wound and is pushed down into the intestinal lumen (Fig 2a), parallel with the intestinal wall, for 2 inches or more It is held in place at the point of insertion (Figs 2 and 2a) by a plain No 0 catgut suture which transfixes both the bowel wall and the tube By the time this suture has been absorbed, the opening has accommodated itself to the size and shape of the tube

The tube, as it makes its exit from the stab wound (Fig 2) lies along the surface of the intestine and passes through the untied ends of the upper traction suture Both the upper and lower

Fig 5 Introduction of nourishment by Triumph syringe, applicable to jejunostomy or gastrostomy Note stopcock on tube, which is closed except when nourishment is being introduced

traction sutures are now held on tension, and as a result of this maneuver there is formed a channel or groove in which the catheter lies The ridges forming the sides of this groove are whipped together at the top over the catheter with a continuous Lembert suture of silk (Figs 3 and 3a) The serosal coat of the intestine thus forms a snug channel in which the catheter lies The infolding is carried down well beyond the point of entry of the catheter so that any leakage into the abdominal cavity is guarded against. The lower traction suture is now tied and cut The upper suture is passed through the peritoneum the transversalis fascia and the posterior sheath of the rectus muscle before it is also tied and cut By this transfixion stitch the upper end of the intestinal channel is attached to the peritoneal surface of the wound The attachment is made at any convenient point in the incision there being less tension, as a rule if the tube makes its exit through the middle of the incision

6. Closure is effected in tiers The peritoneal layer is closed by a continuous stitch of chromic No 1 catgut (Fig 4) and the anterior rectus sheath is closed with a series of silk mattress sutures, placed from a quarter to an eighth of an inch apart. This layer of sutures serves as a precaution against wound rupture and evisceration, an accident peculiarly likely to happen in aged and debilitated patients in whom the operation is frequently done The skin is closed with Michel clips. The tube is clamped with a stopcock (Fig 5) or a pair of forceps and is opened only when nourishment is introduced

COMMENT

The Eiselsberg Witzel technique, which has just been described, is a simple, quick method of creating a permanent, water tight fistula for feeding purposes. The problem is not how to perform this operation but whether to perform it and when to perform it It is a procedure of desperation as we have already intimated, and it should be resorted to only when no other surgery is possible. Its field, obviously is very limited Its usefulness is confined to those cases of gastric malignancy in which the lesion is obstructive and is so located or is of such an extent that the curative operation of gastrectomy or the more useful operation of gastro-enterostomy cannot be done Balfour suggests, in addition that jejunostomy be done in the occasional case in which there is some doubt as to the exact nature of the gastric lesion, and resection, for some reason, is impossible.

Benedict's suggestion in 1898 that jejunostomy should supersede both gastrostomy and gastro-enterostomy would find small approval today There is still logic in his arguments, however that a stomach invaded by a malignant process is not capable of sound digestion and that a malignant lesion even at the cardia, is likely to be further aggravated by the process of gastric digestion Benedict s indications may be too liberal, but there is no doubt that the operation is sometimes justifiable for in many cases the alternative is permitting the patient to starve to death before one s eyes. The choice is always a difficult one Jejunostomy does nothing but delay the inevitable end and sometimes does not delay it for long It does, however relieve pain, and it does eliminate the tortures of hunger and thirst, so that death comes in a kindlier fashion For that reason it should probably be done more frequently than it is, and most certainly it should be done earlier than it is Unfortunately it is not usually given any consideration until the patient is exhausted from starvation and cachexia, and it is these factors, rather than the procedure itself which are responsible for its high mortality

Pre-operative preparation is not necessary A patient about to starve to death should be operated on without delay Postoperative care, aside from the usual measures which would be employed under any circumstances, consists chiefly of attention to the tube and care in the administration of nourishment The tube should not usually be disturbed unless it becomes clogged or unless it slips out In either of these contingencies it should be lubricated with some sterile oil or jelly before it is re-introduced If the channel has been made sufficiently long, the opening in the bowel will be closed by *vis a tergo* when the tube is out, and leakage cannot occur Re-introduction is easily accomplished by gradual, gentle pressure

Water can be given in small quantities through the tube within an hour or two after operation, and feeding can be begun within 6 hours The ideal diet should contain all the essential food elements, and should be at the same time bland, non-irritating, and easily digestible Such a diet, as Wolfer points out, was devised by Ivy and his associates, and to them must go the credit for studying the subject of jejunal digestion in all its details and for devising a diet which is ample for nutrition, which preserves the water balance of the body, which prevents intestinal irritation, and which avoids deficiency states Their formula includes milk, cream, sugar, flour, peptone, Ringer's solution and water, to which are added once a day, to supply the necessary vitamins, orange juice, egg, viosterol oil, Haliver oil, and yeast It is also recommended that gastric juice obtained by aspiration of the stomach should be mixed with the pabulum

The secret of success in jejunal feeding is the administration of the formula in small quantities at short, regular intervals, and at a rate which does not exceed the rate of the passage of the food from the stomach into the intestinal tract in the normal process of digestion The amount of food should be increased very slowly, and intestinal cramps, diarrhea, nausea, or similar symptoms should be taken to indicate that too much food is being given at one time or that it is being given too rapidly

We have found that the barrel of a Triumph syringe serves as a very satisfactory funnel for the introduction of the food (Fig 5), and this method has the added advantage that the patient can feed himself as soon as he is able to sit up or move about If the catheter has been introduced sufficiently far into the bowel, leakage or backflow of the food cannot occur, and if the jejunostomy channel has been made sufficiently long, digestion of the abdominal wall by the jejunal juices is an unlikely contingency

These are the cardinal points in the operation of jejunostomy It is a procedure of despair, but at least there is this to be said for it, that if it is done before the patient becomes too weak to endure any surgery, it is not in itself a lethal operation and it makes the final days of life more tolerable by freeing the patient from the suffering of hunger and thirst and pain Furthermore, if the malignancy is of the slowly advancing type, and if the operation is done at an elective time, there is no reason why feeding cannot be continued almost indefinitely by this route, with a corresponding prolongation of life

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REPAIR OF THE LIGAMENTS OF THE KNEE

Report of a New Operation for Repair of the Anterior Crucial Ligament

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RUPTURE or impairment of function of the crucial, medial, and lateral ligaments is of rare occurrence when compared with injuries of the semilunar cartilages. Acute rupture of these ligaments is often united by conservative measures and undoubtedly there are instances of practically normal function in spite of non-union or elongation which is an equation of individual compensation. However continued disability with instability and evidence of slight derangement followed by acute symptoms from mild trauma, may be solely caused by permanent impairment of these structures. No knee is as efficient or as normal when there is deficiency of these ligaments and repair is indicated when there is only slight disability especially in athletes and laborers, if it can be accomplished by a short and simple procedure.

English observers recognize injuries of the ligaments, and operative measures have been devised by Hey Groves and others, for their repair but, as expressed by Mr Naughton Dunn and Mr Rowley Bristow in their recent articles read in this country, they do not regard injury of these structures of much consequence. However it is admitted that the excision of an offending cartilage does not give 100 per cent excellent results the percentage in a large series of cases varies from 80 to 90 per cent Some of the failures can be attributed to error in operative technique and traumatic arthritis induced by repeated injury to the joint from a detached cartilage, but there is undoubtedly a small percentage which present symptoms of sudden displacement or locking not so severe as in a typical cartilage but quite definite after the removal of a displaced cartilage Occasionally normal semilunar cartilages are found at operation associated with undue laxity or rupture of the crucial or lateral ligaments Also, there is a small percentage which present symptoms of relaxed ligaments without definite signs of displacement or injuries of the cartilage Exploration of such joints is often made with the removal of a relaxed cartilage' or a fat pad, without relief

However when there is a rupture of a ligament or undue relaxation following partial rupture, there is in most instances displacement or fracture of one of the cartilages Impairment of the anterior crucial and medial ligaments is associated with injuries of the internal cartilage, while impairment of the posterior crucial and lateral ligaments is associated with injuries of the external semilunar cartilages.

In a survey of 183 cases of derangement of the knee-joint there were 30 in which there was sufficient evidence of ligamentous impairment to warrant operative procedures to repair these structures

Only the anatomy of the lateral, medial, and crucial ligaments of the knee joint will be briefly reviewed

The medial or internal lateral ligament is attached above to the femur just below the adductor tubercle and below to the posterior portion of the inner aspect of the tibia to approximately 1½ inches below the joint line. This ligament is situated well posteriorly and is about 3½ inches long and from 1½ to 2 inches wide. It is intimately associated with the internal semilunar cartilage and some of the fibers of the vastus internus are attached to the medial surface

The lateral or external ligament of the knee joint is divided into two parts, the anterior or long ligament and the posterior or short ligament The anterior rises above from the external condyle of the femur just anterior to the insertion of the external head of the gastrocnemius and is inserted below into the head of the fibula anterior to the styloid process. This ligament is a thick cord about 2 by 3 inches in length The posterior or short ligament arises from the external condyle of the femur posterior to the long ligament and is inserted into the styloid process of the fibula Both ligaments are separated from the joint by the popliteus tendon and are not in any manner associated with the external semilunar cartilage

The location of the lateral ligament is parallel with the medial ligament well on the posterior aspect of the joint therefore, the medial and the lateral ligaments in addition to the limiting lateral and medial movement, limit extension of the knee-joint, and are thus on tension when the joint is fully extended When a normal knee is fully extended, no motion to either side is possible as both ligaments are on tension

The anterior crucial ligament is attached below into the upper surface of the tibia just anterior to

the spine of the tibia, and above into the posterior portion of the inner surface of the external condyle of the femur There is an attachment to the external cartilage at the lower extremity of the ligament The posterior crucial ligament is attached below to the upper surface of the tibia posterior to the spine and the posterior capsule and passes upward, forward, and mesial to the anterior portion of the intercondylar notch, where it is attached to the anterior portion of the external surface of the internal condyle of the femur A small ligament passes from the posterior portion backward to be attached to the external semilunar cartilage, which is known as the ligament of Wrisberg

The anterior crucial ligament prevents hyperextension and is tense when the knee is fully extended The posterior crucial ligament prevents backward displacement of the tibia when the knee is flexed and is tense in extreme flexion

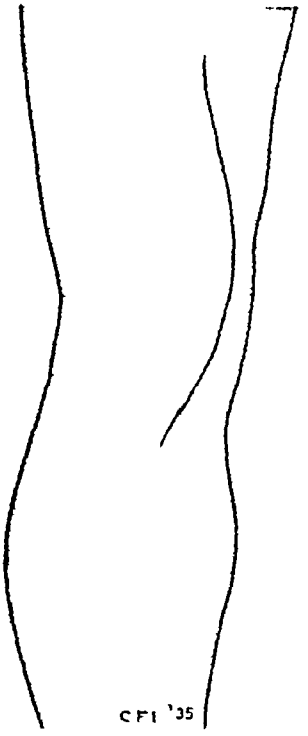

Fig 1 Long medial incision giving access to anterior compartment of the knee joint

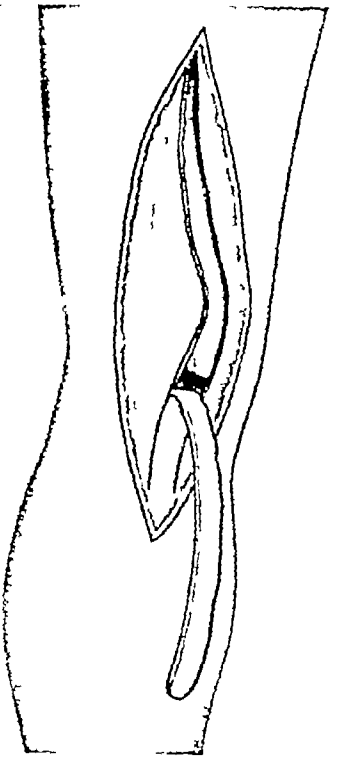

Fig 2 Dissection of strip from tendon and capsule according to the description given

The most frequent mechanism of injury to the mesial and anterior crucial ligament of the knee-joint is the same that causes injury to the internal semilunar cartilage, slight flexion with sudden abduction and external rotation of the knee The most frequent mechanism of injury to the external or lateral ligaments and the external semilunar cartilage, are forces in the reversed direction, slight flexion, adduction and internal rotation Sudden hyperextension, as in the tackling of a leg from the anterior aspect in football, may cause hyperextension with injury or rupture to the anterior crucial ligament, or where the limb is fixed below the knee and the knee is hyperextended with the momentum of the weight of the body in action, as may occur by stepping into a post-hole Rotation, twisting and shearing forces in the knee will rupture one or both crucial ligaments and also the mesial and lateral ligaments

When there is a displacement of the internal cartilage, subsequent injuries can obviously injure the anterior crucial and the mesial ligaments, the latter being intimately associated with the internal cartilage In fact, in all injuries of the internal cartilage there is almost always definite evidence of trauma to the internal lateral ligament, as denoted by tenderness over the attachments and often throughout the ligament

The status of the mesial and lateral ligaments of the knee-joint is brought out in the routine examination with the knee fully extended, if the ankle is grasped with the right hand and the thigh fixed with the left Lateral, rocking motion of the leg by the right hand will give excess motion externally if the internal or mesial ligament is ruptured or elongated, if the lateral ligament is ruptured or elongated, excess motion can be elicited internally Examination of both knees should be made for comparison, as there are certain loose-jointed individuals in whom undue motion is present

If the anterior crucial ligament is elongated or ruptured, the knee will glide forward on the tibia when flexed to a right angle, and to some extent in full extension when traction is made on the calf of the leg with both hands Frequently the excursion will be as much as ¾ of an inch In all cases of complete rupture this test is definitely

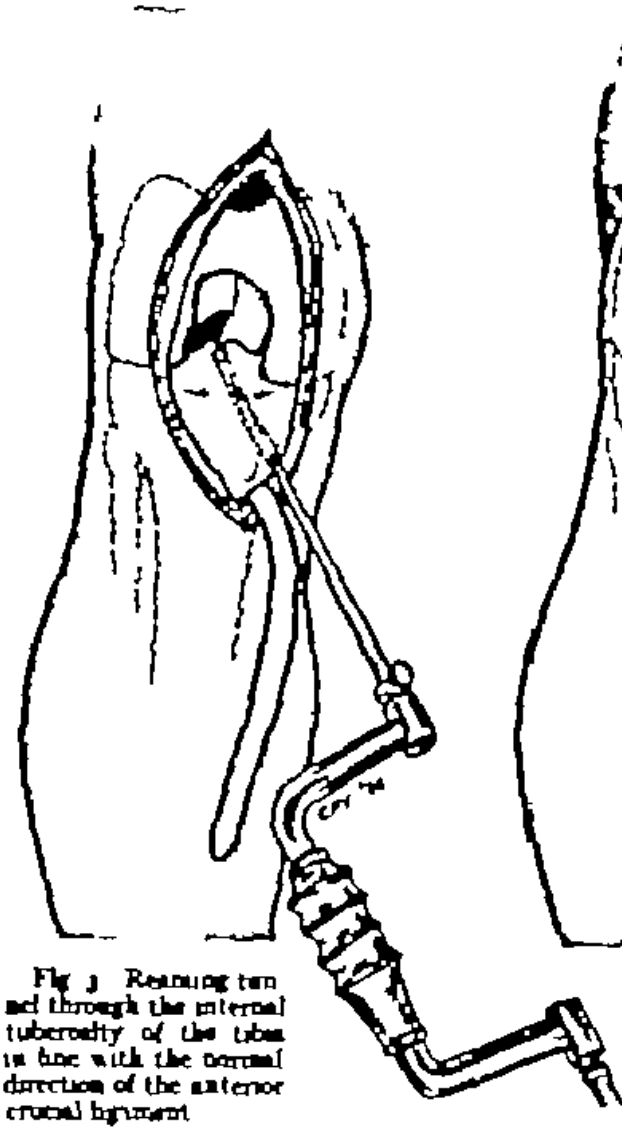

Fig 3 Reaming tunnel through the internal tuberosity of the tibia in line with the normal direction of the anterior crucial ligament

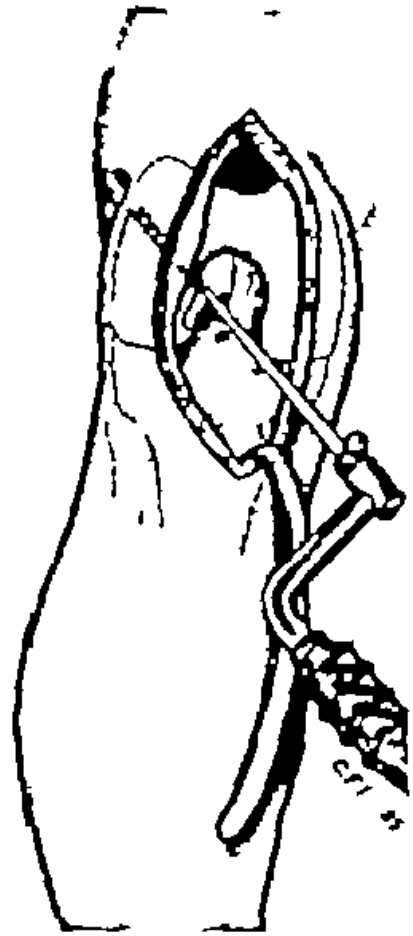

Fig 4 Drilling tunnel in the external condyle of the femur in line with the direction of the anterior crucial ligament

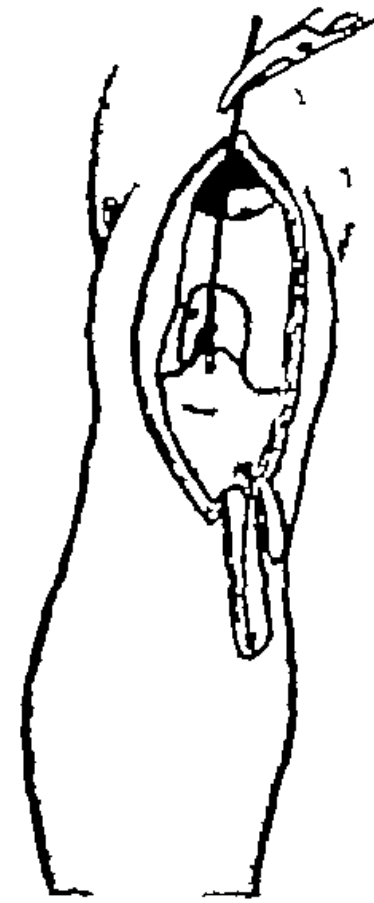

Fig 5 Insertion of wire loop through tunnel in tibia, engaging end of strip

positive In impairment of the posterior crucial ligament the tibia will glide backward on the femur with the knee in flexion. When both ligaments are severed as in complete dislocation of the knee joint and after severe torsion force the tibia can be made to glide backward and forward However in most injuries of this type there is usually so much reaction in the joint and extra articular structures with formation of fibrous tissue, that there is rarely resulting instability and only conservative measures are necessary

I have seen no instance in which the external or lateral ligament or the posterior crucial ligament was causing sufficient disability to warrant operative measures, though I do not doubt that there are instances in which such measures are required The reason that the posterior crucial and lateral ligaments are rarely injured is that the mechanism which causes such injuries is of much less frequent occurrence, and also that the lateral ligaments are not connected so closely to the external semilunar cartilages as the mesial ligaments to the internal cartilage.

Further discussion will be confined to the operative technique for repair of the mesial and the anterior crucial ligaments The technique for the repair of the mesial ligament was described in SURGERY GYNECOLOGY AND OBSTETRICS, February 1935,[1] and is as follows

A skin incision is made parallel with the quadriceps tendon, the patella and patellar tendon, from to 3 inches above the patella to just below the tibial tubercle The deep fascia is incised and the capsule exposed A curved incision parallel with the patella and the upper surface of the tibia is made into the knee joint if internal impingement is suspected and such attention given as may be required, after which the joint is closed The repair of the ligaments is accomplished by diverting from the inner aspect strip of fascia lata, about 0 5 inch in width and 4 inches in length, from above down to a point about opposite the center of the inner aspect of the internal condyle of the femur T parallel incisions about inch in length and about inch apart are next made through the deep fascia and pro-

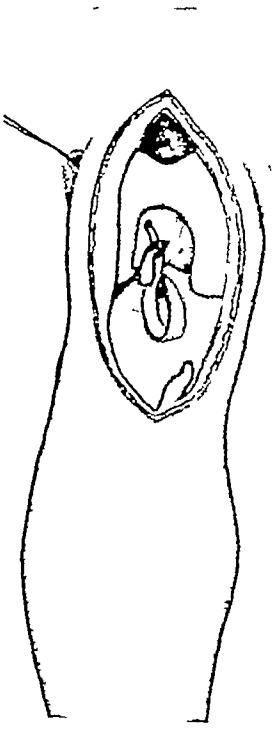

Fig 6 New ligament drawn through tunnel in the tibia

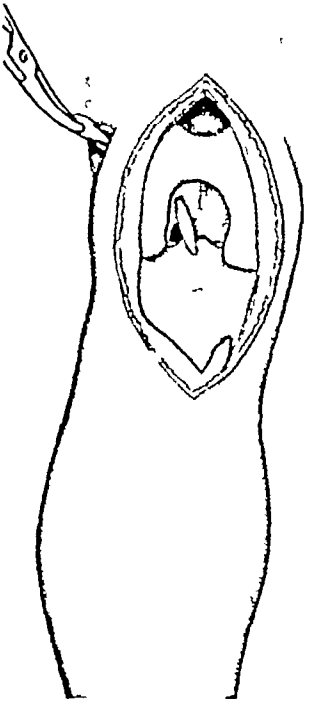

Fig 7 New ligament drawn through tunnel in the external condyle of femur and made taut with the knee flexed about 150 degrees

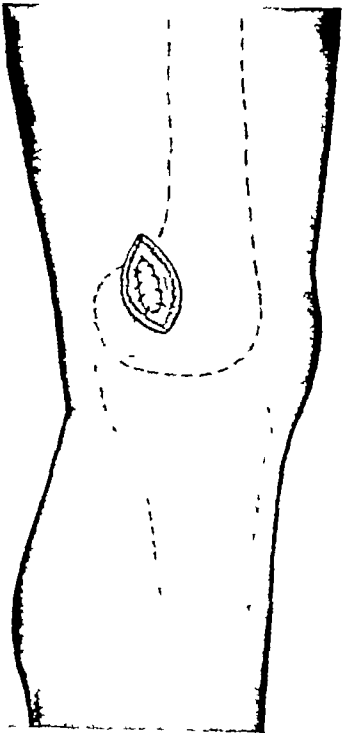

Fig 8 Attachment of superior extension of the ligament to the periosteum and fascia lata

osteum, about 1 inch below the upper extremity of the tibia and parallel with the joint line If the tissue is not sufficiently firm, a tunnel may be made in the tibia at this point. An artery forceps is then passed through the lower incision close to the knee, emerging through the upper incision The upper end of the fascial flap is grasped by the forceps and brought through the tunnel in the dense fascia and periosteum After this the ligament is drawn tight and stitched as high as possible to the margin of the fascia lata from which it has been dissected The limb is held extended and forcibly adducted during the operation By passing the fascia through the tunnel a very accurate pulley action can be made, which permits effective tightening or tautness of the capsule

Apparent impairment of the mesial and lateral ligaments is frequently observed after depressed fractures of the mesial and lateral tuberosities of the tibia Such fractures do cause instability which is entirely due to loss in continuity of bone and not severance of the ligaments Correction of this condition can be secured by a wedge-shaped osteotomy with the transplantation of bone on the depressed side after restoration of the anatomical alinement by elevating the tibial plateau to the normal plane

Only rudiments of the crucial ligaments remain after complete rupture, therefore, a complete replacement must be made with other living tissues of suitable tensile strength In the past we have always employed a pedunculated strip of fascia lata from the outer aspect of the same thigh to replace the anterior crucial ligament, as described by Hey-Groves Following this procedure we have had very satisfactory results, but there was often too much local reaction, which made us think that possibly the procedure, often associated with removal of the internal cartilage, was too much surgery to one extremity Therefore, the following operative technique was devised

A longitudinal curved incision about 6 inches in length is made parallel with the quadriceps tendon, the patella, and the patellar tendon for complete exposure of the knee-joint Dissection is made into the joint cavity throughout the entire incision and the interior of the joint inspected, the cartilage is excised if impaired If the crucial ligament is severed, which can usually be determined on inspection, repair is made by dissecting

a long pedicle strip of fascia capsule and tendon from the lateral edge of the incision about ⅓ of an inch in diameter and 8 inches in length. It is dissected from above downward to the attachment of the capsule to the tibia. This strip contains very strong tendinous tissue from the medial border of the quadriceps and patellar tendons. A 6 millimeter drill hole is then made from a point on the anterior internal surface of the inner tuberosity of the tibia about 1¼ inches below the joint and emerges in the joint at the normal lower attachment of the anterior crucial ligament just anterior to the spine of the tibia. The same drill is then inserted into the intercondylar notch through the posterior portion of the external condyle of the femur emerging under the skin above and posterior to the external condyle. A 3 inch incision is then made over the point of the drill with dissection down to the bone at this point. A rustless steel wire loop is then passed from above downward through the drill hole in each bone and the end of the pedunculated flap brought through to the superior exit of the tunnel in the external condyle of the femur. The flap is now drawn very taut with the knee in about 140 degrees flexion. About 3 inches of the strip should extend beyond the tunnel and is stitched to the periosteum and fascia lata. Both wounds are now closed in routine manner and a posterior splint applied with the knee in full extension, which further increases the tension on the new ligament. The ligament replaces anatomically the anterior crucial ligament, and there should be no undue anterior gliding of the tibia when the ligament is attached above. The operation requires only a few minutes and is attended with much less local reaction than other measures we have previously employed. The after-treatment consists in fixation by a posterior splint for a period of 5 weeks, when active and passive motion is instituted.

There were 30 cases, as above stated, which required repair of ligaments, 12 for rupture or evidence of laxity of the medial ligament and 18 for rupture of the anterior crucial ligament. In only 1 was the procedure carried out for undue laxity of the anterior crucial ligament.

The operation as just described for the repair of the medial ligament, was employed in 6 cases, 3 of which gave perfect results and in 3 it is too early to determine the end-result. Of the 5 in which older procedures were employed, 3 were excellent results, 1 complained of some pain and disability after 2 years, but was improved as compared with former condition. One could not be traced.

Of the 17 cases in which the anterior crucial ligament was ruptured, the operation described was used in 9 with apparent excellent results, but more time should elapse before conclusions can be reached. Of the 30 in whom ligaments were repaired, 9 were college football players and their education depended largely upon their return to the game. Seven of them were able to return the following season, from 6 to 10 months after operation, though they were apparently normal after 2 or 3 months. The result in 1 is too early to report. One case, a farmer had a second injury with apparent rupture of the transplanted fascia lata about 6 months after operation, and is a probable failure. The others had excellent results. In 5 cases of rupture of the anterior crucial ligament in which the fascia lata was employed, a large hematoma occurred, which delayed healing but did not appear to affect the end-result. In 1 a superficial abscess appeared over the thigh where the fascia lata was removed, but healed promptly after drainage. Two cases observed immediately after injury are not considered in this series. In 1 case the ruptured anterior crucial ligament was sutured with excellent result, and in 1 the ruptured medial ligament was sutured with excellent result.

The advantages of the procedures described are their extreme simplicity, minimum trauma, shorter incisions, and decrease in the time of operation though excellent results may be secured by other methods herein mentioned.

The repair of these ligaments is more urgent in athletes and in those whose occupation requires strenuous labor. However in a small proportion of all traumatic knees, possibly 10 per cent, restoration of ruptured ligaments will materially improve the end-results, especially if the procedures employed can be carried out rapidly and without undue intra-articular and extra-articular reaction.

EWING'S SARCOMA (ENDOTHELIAL MYELOMA)

Case Report with Necropsy

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MUCH has been done through the cooperative efforts of surgeons, pathologists, and roentgenologists in the past decade to clarify the many controversial issues in the field of tumors of bone. That much more work needs to be done is clear to anyone who has read the case reports and discussions concerning the clinical and pathological entity described by Ewing in 1927 under the name of "diffuse endothelioma of bone." Since that time fairly numerous case reports have appeared, most of them in the American literature, under various titles such as Ewing's tumor, Ewing's sarcoma, endothelio-myeloma, diffuse endothelioma of bone, undifferentiated round cell sarcoma of bone, etc. The diagnosis in most of these cases has been based upon skiagraphic evidence and microscopic examination of biopsy specimens or even upon clinical history and skiagrams alone. Relatively few of the cases have come to necropsy. Kolodny, in his monograph on bone sarcomas, says: "As a general rule the patient is taken home before termination where he remains until death; necropsies of such patients are scarce." In 1933 Melnick found only five postmortem reports in the literature to which he added one. At least 4 more cases have been recorded in the literature during 1934, 1 by De Santo, and 3 by Connor. Even among these there are some which include insufficient detail and in one of them (Sycamore) the diagnosis was not supported by the histopathological findings. In an excellent critical review of the subject, Hirsch and Ryerson present convincing evidence to support the opinion that many published cases of so called Ewing's sarcoma are really bone metastases from primary carcinomas of the lung. Their analysis of the cases published as endothelioma of bone prior to 1922 shows that none of these can stand, on the basis of the data given, as unquestionable primary tumors of bone and in many cases the descriptions mark them almost certainly as metastatic carcinomas. Colville and Willis: "strongly suspect that adrenal neuroblastomas will prove to be the primary growths in many of the cases."

In view of the varied histological picture presented by different cases of Ewing's sarcoma and the possibility of confusion with certain metastatic tumors, it seems wise to base generalizations with regard to this type of tumor upon data derived from cases that have come to necropsy. In such cases one can at least exclude nephrogenic neoplasms (hypernephromas), adrenal neuroblastomas, and bronchogenic carcinomas, provided the dissection has been carefully done and the findings recorded in sufficient detail. When the lungs contain large or extensive metastases it is not always possible to exclude beyond the shadow of a doubt the existence of a small bronchial carcinoma, and a unilateral distribution is strongly suggestive evidence in its favor. In the case here described the equal symmetrical distribution of metastases, the uniformity of size of the tumors in the lungs, and the lack of demonstrable involvement of any of the bronchi argue strongly against this possibility.

CASE REPORT

No. 98041, Evanston Hospital. A married white woman, aged 23, dress designer, was first seen at home on January 14, 1933. She was lying on her left side with both thighs flexed, complaining of severe pain in the right sacroiliac region and in the right leg. The temperature was 100.4 degrees, pulse 110. A sensitive spot with some swell

Fig. 1. Roentgenogram of pelvis made 10 weeks before death. The earliest involvement was in the left sacroiliac region. Diffuse involvement of vertebræ, innominate bones, sacrum, and heads of both femurs is shown. The skull, ribs, clavicles, and sternum were also involved at this time.

Fig. Sagittal section of upper thoracic spine (left) small piece of tumor from left innominate bone (*upper* right) with an irregular area of necrosis in its middle one third and surface view of rib (lower right) with periosteum removed to show metastatic tumors

Fig. 3 Medial aspect of left lung Tumor nodules are visible in the parenchyma of the lung and in the hilar lymph nodes on the left of the open mediastinum and the extensive pleural involvement is shown on the right

ing was found over the right sacro iliac joint The patient was unable to move on account of pain and with difficulty was turned on her back She would not permit the thighs to be extended on account of the severe pain She said that she had suffered three similar attacks during the past year but previously the pain had been on the left side This was the first attack in which the right side was involved An X-ray film, made October 31 1931, was in the possession of the patient with the following report attached

Lumbosacral spine presented lateral curvature Definition of sacro iliacs was maintained but left presented some adjacent density increase and lipping of outer border at lower extremity of possible osteoarthritic significance

The patient stated that she had been under treatment for an acute arthritis of the sacro iliac joint for several weeks In order that a more thorough study of the case might be made and definite diagnosis arrived at if possible, the patient was sent to the hospital on the next day

On admission she had temperature of degrees, pulse so, blood pressure 3–70 The following history was obtained

She had been well until February 932, with the exception of infrequent colds and occasional attacks of tachycardia and palpitation About a year ago she had fallen down stairs injuring her back, especially in the region of the coccyx, but at the time there was no external evidence of injury In February 932, pain developed in the left sacro iliac area, of moderate severity accompanied by pain down the thigh She received treatments by an osteopath and after month the pain disappeared There was no swelling and no disability and the recovery was apparently complete In the following July another similar attack occurred which was somewhat more severe and lasted about a eek T o months later (September, 1931) there was severe attack during hich the tissues in the region of the sacro-iliac joint became swollen and painful, with shooting pains dow the leg and some weakness in walking With this attack there was some elevation of temperature Again the condition improved and the swelling seemed to disappear In October the third attack began ith great pain and swelling over the left sacro-iliac area, inability to all fever sleeplessness, nausea, and nausheats and pain dow the back of the leg This time the pain, swelling, and disability were persistent but the swelling on the left side had become less tender during the past month During the last weeks similar attack had occurred on the right side ith pain along the right sacro-iliac joint and in the lower part of the spine This attack had been of the same character accompanied by pain in the right leg, but was more severe than the attacks on the other side She had lost 15 pounds during the past year

At the time of admission to the hospital distinct, hard swelling could be felt along the left sacro-iliac joint and smaller but more sensitive swelling in the right sacro iliac area New X ray films were made, with the following report by Dr J T Case

It is very interesting that the films made October 31, 931, showed apparently normal bone findings for the lumbar and pelvic regions and upper femora At the present time we find after period of fever tenderness, hard swelling over the left sacro-iliac area, a marked condition of osteoporosis involving the left innominate bone, the head and upper end of the left femur and to considerable extent the right innominate bone The last lumbar vertebra

Fig 4, left. Low power photomicrograph from fibrous portion of biopsy specimen Strands and small islands of tumor cells are scattered through the dense fibrous mass In this area the cells were small and uniform with clear cytoplasm and slightly resembling metastatic hypernephroma cells

Fig 5 Another area from the biopsy specimen showing lobulation of tumor cells and small trabeculæ of immature bone In some places it was difficult to distinguish osteoblasts from tumor cells

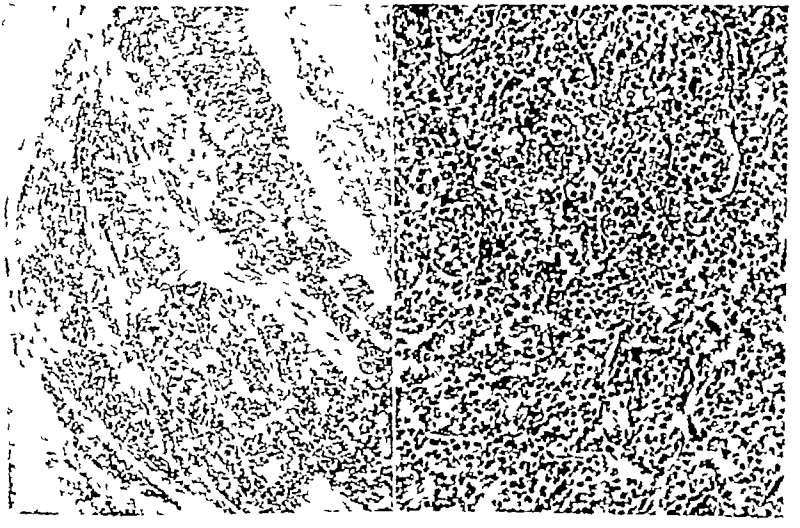

Fig 6, left Low power photomicrograph from the center of the tumor of the left ilium, adjacent to a large area of necrosis and fibrosis (on the left of the figure) The tumor cells are arranged in fascicles between slender fibrous strands

Fig 7 Higher magnification of section shown in Figure 6, showing the uniform size and structure of the cells The small clear spaces between the cells are blood capillaries and (probably) lymph channels

Fig. 8, left. High magnification of section from vertebra. The cells are less uniform than in the primary tumor; the arrangement compact and mitotic figures fairly numerous (four are visible in the figure).

Fig. 9. Section from the advancing margin of a metastatic tumor in the vertebral bone marrow. Here there is much more variation in size and shape of tumor cells than in any part of the primary tumor. A few bone marrow cells (dark nuclei in the picture) have been isolated in the mass of rapidly growing tumor cell.

Fig. 10, left. Low power photomicrograph of lung illustrating lobulation produced by polypoid growth of tumor in alveoli. The perivascular lymph spaces are filled with tumor cells.

Fig. 11. Polypoid mass of tumor tissue in a small bronchus. The tumor is richly supplied with blood capillaries.

seems to be sharing this process of osteoporosis. In the absence of any primary carcinoma, demonstrable, I would consider that this ought to be looked up from the standpoint of hyperparathyroidism.

The more important clinical laboratory findings at this time consisted of the following: Serum calcium, 8.5 milligrams; inorganic phosphates, 3.2 milligrams. Bence-Jones protein and Kahn negative; urine showed no Bence-Jones protein. The sedimentation rate of the oxalated blood was 29.5 millimeters an hour.

Although the initial course and early X-ray examination, which showed changes in the sacro-iliac joint, were compatible with a diagnosis of osteomyelitis, the later film introduced another possibility. The clinical laboratory findings tended to include hyperparathyroidism. It was felt that biopsy was necessary to differentiate the lesion further.

Accordingly, on January 18, 1941, an incision was made below the posterior part of the left iliac crest and along the sacro-iliac joint. Before the bone was reached, a mass of

grayish, slightly vascular, dense tissue was found protruding into the muscle. A wedge of this tissue was removed. The cortex of the ilium was so fragile and soft that a probe could be pushed through it. With a curette a piece of bone from the ilium immediately beneath the protruding mass was removed The incision was then closed. It is of interest that the biopsy wound closed and healed quickly by first intention and there was no sign of recurrence in the wound until just before the patient's death in the following June.

Extract from microscopic report "Most of the tumor cells are pale, polyhedral with round or oval, pale nuclei only occasionally showing small, dark nucleoli. In the lobules the cells are packed close together without any intercellular substance, but some of the lobules are further subdivided into alveolar structures and cords by slender fibrous trabeculæ. In addition to the pale cells there are very small irregular masses and strands of hyperchromatic cells which do not have clear cell boundaries and the cytoplasm is so darkly stained that the nuclei cannot be clearly distinguished.[1] One section contains a few, scattered, atrophic, skeletal muscle fibers near the advancing margin of the tumor Mitotic figures are moderately numerous in the more cellular areas (5 to 8 per high power field)

Tentative diagnosis "Ewing's sarcoma."

Deep X-ray therapy was attempted but owing to the prostration which followed each treatment it was soon abandoned. For this reason no deductions could be made regarding the radiosensitivity of the tumor

Subsequent X-ray examination of the skeleton showed progressive extension of the disease through the pelvis, into the lumbar spine, the hip joints, the upper ends of the femurs, the ribs, and skull (Fig 1) No radiological examination was made of the small bones of the hands and feet or the long bones of the forearms and legs

The later progress showed a number of interesting clinical developments For instance, there were periods of a week or more when the temperature was normal or subnormal and then, apparently without reason, it would rise to 101 degrees or higher, showing fluctuations which suggested sepsis, receding daily for a week or 10 days and then returning to normal or a subnormal level There were periods of several days, even as long as 2 weeks, during which there was evidence of general improvement with little or no pain and such a feeling of well being that the patient would talk about getting up Not infrequently the period of improvement was followed immediately by severe collapse associated with dyspnea, restlessness, and great variations of the pulse The following abstracts from the progress notes are of interest.

February 28, 1933 "X-rays show an extension of the malignancy with compression of the twelfth dorsal vertebra. For the first time, today she has had focal eye signs The right eye is limited in all external movements the patient is troubled with diplopia A cerebral metastasis seems likely Pulse remains very high"

March 10, 1933 "The eye signs mentioned in the last note cleared up completely after 4 or 5 days She has failed steadily and in recent days has lost more weight, particularly noticeable in the face. Severe lancinating pain has been present for the last few days over the left scapula The patient is clear mentally at times, but lapses into a state of irrationality or stupor Her breathing during sleep particularly at night is at times Cheyne-Stokes in type with long periods of apnea Fever has been absent for 2 days Pulse is very weak but not as rapid as formerly The patient certainly has few days to live."

She did live, however, almost 2 months During this time the left eye became prominent (presumably due to a retrobulbar metastasis), three soft spots, each about the size of a quarter, appeared in the skull, and it was noticed that the size of the tumor in the region of the left hip was increasing very rapidly A few weeks before death a collapse occurred, similar to the previous ones, with unconsciousness, respirations 8 per minute, pulse 48, the patient was thought to be dying However, on the following morning the pulse had risen to 110, respirations to 20 and the patient was sufficiently alert to ask for her glasses and look over a magazine. Three weeks later, 1½ years after the first attack of pain, death occurred during a similar period of collapse The mentality was clear up to the hour of death except while under the influence of morphine

Necropsy The necropsy was performed about 8 hours after death on the previously embalmed body The examination was restricted to the trunk and consequently our knowledge of the degree of involvement of the long bones of the extremities and the bones of the skull is incomplete An abstract of the necropsy record follows

External examination of the body revealed extreme wasting of the soft tissues, flexion deformity of the hip and knee joints and a partly healed decubitus ulcer over the sacrum. The biopsy wound was perfectly healed and the scar was stretched over the surface of a firm, dome-shaped tumor, measuring about 8 by 5 5 by 2 centimeters which protruded from the lateral aspect of the left ilium The scalp was thin and the tumors in the calvarium could be easily outlined by palpation A firm node, 2 centimeters in diameter, protruded from the surface of the left parietal bone about 2 centimeters from the median line, another of about the same size in the right parietal bone, 1 centimeter from the midline, three on the right side and one on the left of the occipital bone, measuring up to 2 5 centimeters in diameter and elevated 2 to 4 millimeters above the surface of the bone. No tumors could be demonstrated by external examination of the long bones of the extremities, although their surfaces could be outlined readily by palpation. The breasts were small and free from tumor masses There was moderate edema of the feet and ankles

When the chest wall was uncovered, numerous firm nodules, 1 to 2 5 centimeters in diameter were seen protruding from the outer surfaces of the first to the sixth ribs, inclusive, on the right side, the first to the seventh ribs, inclusive, on the left side and from the medial end of the left clavicle The tumors were much more prominent and more numerous when viewed from the inner aspect of the chest wall All of the ribs were found to be involved and one showed sixteen separate nodules and fusiform enlargements on its inner surface. One large nodule was attached to the inner and superior aspect of the sixth costal cartilage. When the ribs were split, the tumors were found to be embedded in the cancellous portion, the larger masses having destroyed the cortex, elevated the periosteum and in a few places the periosteum had been penetrated and the fascia and muscle invaded.

Several tumor nodules from 5 to 10 millimeters in diameter projected from the posterior surface of the middle one-third of the sternum. Similar nodules in large number, many of them confluent, protruded from the lateral and anterior surfaces of the thoracic vertebræ. So much of the bone had been destroyed in the bodies of the upper thoracic vertebræ that slices could be removed with a sharp knife and no red marrow could be distinguished on surfaces made by section (Fig 2) The tumor tissue here was similar to that in the ribs and sternum and consisted of a fairly firm, gray to grayish-yellow, homogeneous substance with-

[1] An artefact due to crushing

out gross evidence of retrogressive changes. No protuberances were found on the surfaces of the lumbar vertebrae but on section, several poorly defined masses measuring up to 2 centimeters in diameter were found embedded in the cancellous bone of each vertebral body.

A large, smooth tumor attached to the base of the left fibula and sacrum, involving practically the entire left wall of the pelvis, encroached upon the pelvic organs from the left side. The periosteum was apparently intact over its entire surface. Several yellow areas of necrosis were found on sections made through the middle of the main tumor. Small spicules of bone were encountered in various portions of the tumor but chiefly at its periphery. The crest and anterior portion of the ilium were firm but all portions contained masses of tumor tissue. The cortex of the right ilium was apparently unbroken though reduced in thickness in many places and the cancellous portion was largely occupied by yellow gray tumor tissue.

Visceral metastases. Grossly visible metastases were confined to the lungs and thoracic lymph nodes. The pleural surfaces of the lungs were studded with small and large protuberant nodes which were discrete in the apical portions and in a narrow zone along the hilus of each lung but elsewhere they were confluent and covered practically the entire surface (Fig. 3). In the lung parenchyma the nodes were for the most part discrete and measured up to 18 millimeters in diameter. They were scattered fairly evenly throughout both lungs and replaced approximately one-half of the parenchyma of each. The intervening lung parenchyma was compressed by the tumors and contained a slight excess of fluid. The peribronchial lymph nodes were firm, solidly filled with yellow gray tumor tissue and measured up to 1 centimeter in diameter. The tracheobronchial and paratracheal nodes were enlarged up to 3 by 2 by centimeters and their parenchyma was almost entirely replaced by firm, homogeneous tumor tissue. The lining of the trachea, primary and secondary bronchi was smooth and pale. (The smaller bronchi were examined by cutting the previously hardened lungs into thin slices. Many were compressed by tumor nodules.) Thick cords of tumor tissue, parallel to the blood vessels and bronchi, and probably representing dilated lymph channels, were found in all portions of both lungs.

The thyroid and parathyroid glands were grossly normal. No glandular tissue could be seen in the extremely thin pad of fat which represented the thymus gland. The epicardial fat was thin and gelatinous. The myocardium was red brown and the mitral valve showed slight fibroplastic deformity. The liver was small (about kilogram). No tumor nodules could be found in its substance. The gall bladder and bile ducts were normal. No gross alterations could be found in the stomach, intestine, pancreas, suprarenal glands, kidneys, ureters, urinary bladder, uterus and adnexa, spleen, abdominal lymph nodes, and blood vessels.

Histopathology. All tissues for section were fixed in formol Zenker solution and sections of the tumor were stained with Giemsa, Van Gieson, and Mallory (connective tissue) stains in addition to the routine hematoxylin and eosin.

Bones (ilium, vertebral bodies, and ribs). The tumor is composed of polyhedral cells with oval nuclei and scanty unstained cytoplasm. The nuclei contain fine chromatin nets, coarse and fine granules, and a few large acidophilic nucleoli (Figs. 4, 7 and 8). The cell boundaries are practically indistinguishable in those areas in which the cells are compact but in some places fine cytoplasmic processes can be seen joining one cell to another. The masses of compactly arranged cells are traversed by coarse septa of connective tissue and divided into small, irregular lobules by a network of fine strands of fibrous tissue resembling the form of an irregular honeycomb (Figs. 5, 6, and 7). Within the small lobules, no intercellular substance is present. The fibrous framework contains a numerous fine blood capillaries and a few empty spaces resembling lymph channels (Fig. 7). Small, isolated fragments of degenerated bone are scattered through the tumor tissue and slender trabeculae of newly formed osteoid tissue are found in some of the thick fibrous septa, especially in sections taken from the periphery of the pelvic tumor where remnants of the displaced periosteum can be recognized. In a few places, thick, anastomosing trabeculae of newly formed bone and osteoid tissue are embedded in cellular portions of the tumor at some distance from the periosteum (Fig. 5). In these no lamellar structure is present. Small narrow spaces containing reticular tissue and tumor cells are found in the larger trabeculae. The margins of the trabeculae are lined by cells resembling osteoblasts, arranged irregularly and in many layers. Most of these are considerably smaller than the cells of the periphery. Some parts of the tumor fail to show any lobular arrangement. In these the cells are especially compact and most of them are spindle-shaped. Sections of the pelvic tumor mass (left ilium) contain large areas of coagulation necrosis with actively growing tumor tissue at the periphery (Fig. 6). In the lumbar vertebral bodies the marrow cells are generally hyperplastic with cells of the granulocytic type (myelocytes and myeloblasts) in marked preponderance. The marrow cells are especially numerous and compact at the advancing margins of masses of tumor cells. A considerable number of lymphoid cells and cells resembling plasma cells are mixed with the granulocytes in the hyperplastic areas. There is no indication in the sections that these are derived from the tumor cells.

Noteworthy variation in size of the tumor cells is observed in the region of these advancing margins of secondary tumors (vertebrae and ribs, Fig. 9) in contrast to the uniformity of size in the main tumor mass and especially in the biopsy sections (compare Figs. 4, 6, 7 and 8).

Visceral metastases. Lung. In the metastatic nodules, the lobular arrangement is similar to that found in the bone tumors. The larger nodules have replaced the lung parenchyma so that the alveolar walls and bronchioles have been entirely obliterated; but in some areas the dilated alveolar spaces and small bronchi have been filled in by polypoid masses of tumor cells and their vascular stroma, resulting in a peculiar sharp lobulation in which each lobule represents an alveolar space (Figs. 10 and 11). Small tumor masses are found in the perivascular and peribronchial lymph channels, and in some places they appear to be free in the air sacs. In the central portions of the largest nodules the stroma is increased to such an extent that small groups and strands of tumor cells are isolated in the poorly cellular stroma. The cells of this stroma are small spindle shaped cells resembling fibroblasts.

Peribronchial lymph nodes. The finely lobular structure of the tumor masses is similar to that found elsewhere and there is a suggestion of alveolar arrangement with most of the nodes located at the periphery of the lobule and relatively abundant faintly acidophilic cytoplasm. Intercellular mucoid stroma is abundant in the central part of some of the nodes.

Suprarenal glands. Several small solid masses of tumor cells, some of them in the form of cords within sinusoids, are found in both cortex and medulla. The cortical structures appear normal and the medulla contains abundant chromaffine tissue.

In the kidneys there is evidence of subacute glomerulonephritis, but there were no metastatic tumors in the sections. Both liver and spleen contained an abnormally large amount of hematogenous pigment. Pancreas was normal.

SUMMARY AND DISCUSSION

In summarizing the clinical features of the case, it should be noted that all of the features which have been emphasized as characteristic of this disease were present from the history of trauma to bone in a young individual, followed by symptoms suggesting osteomyelitis with fever, swelling and pain, recovery in a few weeks, attacks recurring at shortening intervals, becoming more severe and finally persisting in some one bone Finally the patient died with tumors in the skull, extremities, spine, ribs, lungs, and lymph nodes, 1½ years after the appearance of the first symptoms (Variations in duration of life from 5 months to 16 years were noted by Kolodny in the Registry material) The skeleton in this case was so extensively involved and the process so diffuse at the time of the second X-ray examination that an osteoporosis due to hyperparathyroidism was suggested

The tendency to widespread diffuse involvement is characteristic of the disease but may be closely imitated by other tumors both primary and metastatic During the same year in which this case was under observation we had opportunity to examine a case of multiple myeloma (myelocytic type) which had showed a strikingly similar roentgenographic picture in the pelvis, ribs, and spine Connor found most difficulty in differentiating metastatic lymphomatous tumors from Ewing's sarcoma

Following diagnosis by biopsy, X-ray therapy was instituted but was soon discontinued on account of the severe prostration which followed each treatment and the rapid spread of the tumor was apparently unaltered by it In some of the earlier publications, the prompt response of Ewing's sarcoma to adequate radiotherapy was emphasized In Connor's opinion this is an erroneous conclusion He believes that in this respect it is much like malignant endotheliomas arising in other tissues and that in radiosensitivity it stands midway between osteogenic sarcoma and highly sensitive tumors such as metastatic lymphosarcoma and neuroblastoma in bone A combination of irradiation and surgery has been found to give the best results in treatment according to Geschickter and Copeland "yielding about 10 per cent of permanent cures "

The effect of biopsy upon the tendency of the tumor to metastasize is a problem which has been much discussed but is still far from final settlement. Geschickter and Copeland are of the opinion that "exploration does not necessarily affect the prognosis in cases in which radical operation or X-ray treatment follows exploration " This is supported by the data recorded by Crowell from the Registry of Bone Sarcoma Of the 9 cases of Ewing's sarcoma with clinical cures of 5 years or more, all were subjected to surgery, 6 were treated by amputation and of the amputation cases 4 cases had 1 or more surgical procedures at some period prior to the amputation Opposed to this view there are many who advise strongly against any incision of the tumor and advise radiotherapy to the tumor on the basis of clinical and roentgenologic diagnosis It must be confessed that had we proceeded on such evidence in this case, the procedure adopted would have been either an exploratory operation in the neck or radiotherapy to the region of the parathyroid glands The difficulties and failures in diagnosis from biopsy specimens have been fully discussed by Kolodny and many others in case reports and reviews of this subject.

Further discussion at this time of the question of histogenesis of Ewing's sarcoma seems futile in view of the scanty evidence presented in the published cases and with such striking variations between individual cases The microscopic evidence in this case seems to favor no particular theory While the formation of new bone was a conspicuous feature in the tumors of the skeleton, there is no direct evidence that the tumor cells themselves were responsible for the laying down of new bone No bone formation occurred in the metastases of the lungs or other soft tissues except the muscle outside of the main tumor where there was abundant opportunity for the displacement of hyperplastic osteoblasts along with the disruption of the periosteum The formation of vascular channels within the intra-alveolar and intrabronchial, polypoid tumors of the lung is not conclusive evidence of angioblastic properties since it is just as reasonable to assume that the vessels of the alveolar walls were appropriated by the tumor cells as they formed the protrusions into the alveolar and bronchial lumina. Furthermore, similar pictures have been observed in other metastatic tumors of the lung where no question of endothelial origin could be raised Likewise, hyperplasia of the cells of the bone marrow at the borders of spreading foci of tumor cells is frequently seen in metastatic carcinoma, in the early stages before fibrosis has appeared, and in itself is no proof that the hyperplastic blood cells are derived from tumor cells No myeloid cells, either immature or mature, were associated with the tumors in the lungs or lymph nodes

The general biological characteristics such as diffuse growth and widespread involvement of the skeleton suggest a relation to multiple myeloma but pulmonary metastases seem to contradict this relationship Connor's view, that the cell of origin

is an undifferentiated mesenchymal cell (reticulo-endothelial cell?) which may become differentiated "into adult reticulo-endothelium, into the hemohistioblast, or into endothelium," which may lay down cement substance and become an angio-endothelioma or which, under other circumstances, may become an osteoblast, is very attractive and serves to bring together the various theories of origin but requires much more proof before the question can be finally settled.

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REGIONAL ENTERITIS (NON-SPECIFIC)

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NON-SPECIFIC inflammatory tumors of the gastro-intestinal tract have been reported at various times in the medical literature but they have been considered medical curiosities rather than well established clinical entities In 1932 Crohn, Ginzburg, and Oppenheimer separated from this group an inflammatory lesion of the terminal ileum which they believed to be a clinical and pathological entity In their first report, these authors described a lesion which, in their series of 14 cases, was limited to the terminal ileum Shortly after their report Harris, Bell, and Brunn reported a case with an inflammatory lesion of the jejunum pathologically identical with the lesion described by Crohn and his co-workers Subsequently, there have appeared in the medical literature rather numerous reports of cases with a chronic non-specific inflammation of ileum, jejunum, and colon Recently Crohn added to his first report 3 cases in which the chronic non-specific inflammatory process he described for the ileum was found in the jejunum and upper ileum He also reports a condition in which the inflammation of the terminal ileum is associated with an inflammation of one or more segments of colon The segments of colon appear fiery red and are covered with exudate, but are separated by wide areas of normal colon It appears that this regional inflammation of the jejunum, ileum, and colon is indistinguishable pathologically from the lesion of the terminal ileum originally described by Crohn and his co-workers Although indistinguishable pathologically, the lesions at different levels of the intestinal tract, on account of their location may give rise to different symptoms Regional enteritis of the terminal ileum, the regional ileitis described by Crohn, may present a clinical picture which differs from the regional enteritis of the jejunum or colon The symptoms likewise vary according to whether the inflammatory process is acute or chronic or whether it is associated with ulceration or stenosis, or both, of the intestine

During the past 2 years we have had 8 cases of regional enteritis In 1 case the inflammatory process was in the lower jejunum, and in the 7 remaining cases the lesion was in the terminal ileum Four of the patients with lesions of the ileum had an acute regional enteritis, 2 had a chronic regional enteritis with stenosis, and 1 had a chronic regional enteritis with an external fistula.

The pathological anatomy of regional enteritis is that of a non-specific inflammation with excessive connective tissue reaction Although the pathological process is continuous and progressive, it can be divided for clinical purposes into three stages (1) acute regional enteritis, (2) chronic hypertrophic enteritis with stenosis of lumen, and (3) chronic enteritis complicated by external or internal intestinal fistula

Acute regional enteritis of the terminal ileum in our series occurred in 4 cases In these patients, as seen at operation, the peritoneal cavity contained a small amount of serous fluid The terminal 15 to 30 centimeters of the ileum was edematous and hyperemic in 2 patients and in the 2 remaining, congested, purplish-red, soggy, and enlarged to about one and one-half times its normal size The process stopped abruptly at the ileocecal valve On the proximal side it disappeared gradually in 2 cases and stopped abruptly in 2 The ileal peritoneum was smooth and glistening The regional mesenteric lymph glands were hyperplastic In the 3 cases that underwent spontaneous resolution the mesentery, although hyperemic at operation, was not thickened or edematous In the case that failed to resolve spontaneously, the mesentery of the ileum was edematous, although the involvement of the ileum grossly appeared about the same as in the cases that did resolve spontaneously It may be that the absence of thickening and edema of the mesentery, indicates that the inflammatory process is still limited to the ileum and perforation of the ulcerative process into the mesentery has not occurred, whereas, the association of a thickened edematous mesentery with a regional enteritis may be indicative of a perforation into the mesentery with abscess formation This tendency toward perforation into the mesentery is more pronounced in the cases of chronic regional enteritis Spontaneous resolution, once perforation into the mesentery has occurred, is probably less likely to take place than if the process is limited to the bowel wall The state of the mesentery of the involved ileum may be, therefore, an indication as to the treatment to be followed, i e whether to resect, shortcircuit, or leave alone

Since most cases of acute regional enteritis are treated conservatively there has been little opportunity to study the changes in the mucosa and the muscular layer of the diseased bowel. Jackman, Erb, and Farmer report cases of inflammation of the terminal ileum, the description and illustrations of which correspond closely to the macroscopic appearance of the ileum in one of our patients in whom diagnosis at operation was acute regional enteritis and who recovered spontaneously. In Jackman's cases, "The mucosa over a wide area had been replaced by a firm hemorrhagic exudate with roughened surface. The transition between the disease and healthy segment was somewhat abrupt. The mucosa was more severely ulcerated along the mesenteric side of the bowel. Microscopic examination revealed a condition of simple intestinal ulceration. The mucosa throughout the affected area had been completely destroyed and replaced by a thick fibrinopurulent exudate. In the bowel wall generally there was an acute inflammatory reaction lessening in degree toward the subperitoneal layer which showed congestion, edema, and interstitial hemorrhages, but few polymorphonuclear cells. This was in marked contrast to the condition in the submucosa and muscle layers where in places the degree of polymorphonuclear cell infiltration approached abscess formation. Evidence of previous acute inflammation of the bowel was present in the form of much dense scar tissue.

The pathological changes in the chronic forms of regional enteritis have been thoroughly studied, since these are the lesions most frequently resected (Figs. 1, 2, 3, 4). When seen at operation the peritoneal cavity contains a small amount of serous fluid. The inflammatory process in the ileum either stops abruptly at the ileocecal valve or continues into the cecum, and extends orally for about 15 to 35 centimeters, gradually shading off into normal intestine. The mesentery of the involved bowel may be 2 centimeters thick. Fistulas are often found between the terminal ileum and adjacent bowel, usually the sigmoid. Walled-off abscesses in mesentery are not rare.

Examination of resected specimens shows the wall of the ileum thickened, as a result of inflammatory hyperplasia of all the layers. This hyperplasia is greatest near the ileocecal valve where the wall may reach three to four times the normal thickness. The mucosa is swollen, the intestinal folds thickened. Along the mesenteric border of the mucosa there are linear ulcerated areas a few millimeters in diameter. In the region of the ileocecal valve, there are areas of papillary and polypoid hyperplasia. The lumen of the ileum is usually constricted, and the narrowing most pronounced in the region of the ileocecal valve. The ulcerations along the mesenteric border in all our ileal specimens showed a tendency toward perforation. This was illustrated by roentgenograms of the specimens taken after distending the ileal lumen with a solution of barium sulphate (Figs. 5, 6 and 7). The earliest perforations were in the form of linear fistulas that began in mucosal ulcers along the attachment of the mesentery and penetrated the bowel wall to the region of the subserosa. As the ulceration progressed, the sinuses penetrated through the bowel wall and led into a common cavity in the mesentery which at operation was found to be an abscess.

During the perforation of these sinuses a neighboring loop of bowel, usually colon, as occurred in Case 5, becomes adherent to the ileum and a fistula becomes established between them. A second mechanism whereby internal fistulas develop is ulceration of a mesenteric abscess into an adherent loop of bowel. The abscesses in the mesentery although usually small, often become large enough to simulate an appendiceal abscess. When these abscesses are drained a persistent fistulous tract may become established between the ileum and the abdominal wall.

The cecum when involved becomes constricted at its distal end by a hyperplastic inflammatory process which appears to extend from the ileum and invade the cecal wall. The thickening of the cecal wall is greatest at the ileocecal valve and gradually diminishes distally into normal cecum and ascending colon. The mucosa of the cecum in our cases showed no ulceration.

Histologically the chronic forms of regional enteritis show no changes to indicate one of the recognized granulomas, such as syphilis, tuberculosis, actinomycosis, or Hodgkin's disease. The mucous membrane of the ileum in our specimens was irregularly ulcerated (Fig. 8). The ulcers were lined by a non-specific granulation tissue which was extensively infiltrated by polymorphonuclear leucocytes. A chronic non-specific granulation tissue extended diffusely throughout the muscular layer and into the subserosa. This granulation tissue contained nodular granulomas which were composed of histocytes and fibroblasts, with an occasional foreign body giant cell and a peripheral zone of lymphocytes (Figs. 9 and 10). In some sections these giant cells contained vegetable fibers. The presence of foreign body giant cells, as suggested by Moschowitz and Wilensky undoubtedly has led many observers to make a diagnosis of hyperplastic ileocecal tuberculosis in cases of chronic regional ileitis.

The pathological process in our patient with regional enteritis of the jejunum consisted of a [illegible] the [illegible] of the jejunum with ulceration and penetration at the [illegible]. The [illegible] was walled off by the [illegible] and adjacent small bowel. The jejunum proximal to the lesion was dilated [illegible] acute [illegible] [illegible] the bowel [illegible]

Regional enteritis [illegible] Barker [illegible] ileum, apparently [illegible] child aged 5 and Brown, Bargen and Weber reported a case in [illegible] [illegible] The [illegible] and the oldest, [illegible] females and [illegible] Crohn, Ginzburg and Oppenheimer and Brown, Bargen and Weber found the [illegible] of males to females [illegible]

The symptoms of regional enteritis according to the classification of Crohn and his co-workers may be divided into four groups: (1) symptoms of acute or subacute abdomen, (2) symptoms of ulcerative colitis, (3) symptoms of chronic obstruction of the small intestine, and (4) persistent and intractable intestinal fistulas that follow drainage of an abdominal abscess.

The symptoms in 4 patients in our series simulated those of an acute appendicitis. Abdominal pain was the outstanding symptom. At the onset, the pain was diffuse and colic-like. Cramps occurred in paroxysms with relative freedom from symptoms between paroxysms. The child aged 7 years in our series, while being examined, had abdominal cramps which doubled him up and caused him to cry. The pain lasted 1 to 2 minutes and then subsided for about 4 to 5 minutes, when it recurred. This colic-like intermittent pain which resembled the pain of an acute intestinal obstruction was present in 3 cases of acute regional enteritis of the ileum that were confirmed at operation. There was no history of diarrhea in any case. The fever in these acute types varied from 99 to 101 degrees F. A moderate polymorphonuclear leucocytosis was present.

Abdominal examination showed tenderness in the right lower quadrant. General physical examination was otherwise negative. This association of the symptoms and physical signs of an acute appendicitis with those of an acute but incomplete intestinal obstruction is very suggestive of an acute regional ileitis.

The symptoms of the chronic form in which the inflammatory process in the ileum has produced a stenosis of the intestinal lumen, are those of a low grade small intestinal obstruction. For a period of months to a year, as occurred in our group, the patients complain of abdominal cramps, particularly after indiscretions in diet. Mild abdominal distention is present. The general symptoms and signs of sepsis, such as loss of weight, anorexia, moderate anemia, persistent low grade fever, and leucocytosis are usually present. One of our patients, besides these symptoms, had repeated attacks of severe right lower quadrant pain associated with a fever of 102 to 103 degrees F and right sided tenderness. These symptoms lasted for about 2 days and then subsided. At operation she had a mesenteric abscess which was walled off by small bowel. The paroxysms of pain and fever were probably due to the gradual extension of the abscess and localized peritonitis.

Physical examination of the abdomen of patients with the stenotic form of regional enteritis of the terminal ileum discloses mild distention and a mass in the right lower quadrant. The mass is most frequently felt abdominally although in one of our cases the mass lay to the right of the uterus and was felt only on pelvic examination.

The patient in our series who had progressed to the fistulous stage gave a history of drainage of an abdominal abscess. Subsequently, a sinus persisted and resisted all forms of medical treatment. Recovery followed resection of the diseased bowel and fistulous tract.

Although Crohn and his co-workers report the frequent occurrence of diarrhea and symptoms simulating an ulcerative colitis, only 1 of our patients gave a history of diarrhea and none noted gross blood in the stools.

The symptoms in our case of regional enteritis of the jejunum were those of an intestinal obstruction of gradual onset. Within 3 weeks of the onset the patient developed symptoms of an acute intestinal obstruction with feculent vomiting, abdominal distention, visible peristalsis and obstipation.

Roentgen-ray examination of the gastro-intestinal tract of cases with regional enteritis of the terminal ileum is entirely negative, or shows a filling defect in the terminal ileum. Barium enema usually fails to show any changes in the colon. The head of the cecum in some cases is narrowed, especially in the region of the ileocecal valve. If the ileocecal valve is incompetent, a filling defect in the terminal ileum is noted. A barium meal usually gives more definite findings

When our cases of acute regional enteritis that subsided spontaneously were examined roentgenologically 1 month after operation the terminal ileum showed only the rapid intermittent passage of barium through it. Three months after operation the involved ileum appeared normal. The case of acute regional enteritis of the ileum that progressed to the chronic form developed a filling defect just proximal to the ileocecal valve. In the fully developed chronic stenotic forms, barium meal usually shows a filling defect in the terminal ileum with a mild ileal stasis and distention proximal to the defect. If the constriction is limited to the last few centimeters of the ileum, and only partially occludes the bowel the filling defect may be overlooked. In the chronic cases in which the inflammatory process involves a longer loop of ileum, the involved loop appears as a narrow rigid tube in which valvulæ conniventes are not seen (Figs. 11 and 12) In the more advanced cases with still greater stenosis, the involved loop s lumen roentgenologically resembles a cotton string. Kantor calls this the "string sign," analogous to the "string sign" described by Crane in the spastic colon.

Fistulous communication between the ileum and colon may lead to delayed motility or to a mild constriction at the site of the fistula. Careful roentgen examination with a barium enema may disclose a fistula between the colon and terminal ileum. Injection of an opaque medium such as iodized oil, into an external fistula which results from a regional enteritis should show the connection between the fistula and the small intestine, usually terminal ileum.

The treatment of the acute types of regional enteritis depends upon the stage of the inflammatory process. If the inflammation is limited to the terminal ileum and the mesentery is uninvolved, resection may not be necessary since the process may resolve spontaneously If however, the mesentery is thickened, indurated, and edematous, the ulceration of the ileum may have extended into the mesentery In these cases, spontaneous resolution is less likely to occur so that a short circuiting operation or a resection of the involved bowel is the better procedure.

In 3 cases of acute regional enteritis, the terminal ileum alone was involved without an associated edema or thickening of the mesentery All these cases resolved spontaneously Rockey Erb, and Farmer report similar cases of spontaneous recovery in children in whom the terminal ileum was edematous and injected In 1 patient of ours the mesentery of the involved ileum was thickened and edematous. Believing that the process would go on to spontaneous resolution, we did an appendectomy to simplify subsequent diagnosis and closed the abdomen. The patient's symptoms recurred 3 weeks later and became progressively more severe. A resection of ileum, cecum and ascending colon was done. This operation was followed by recovery

The treatment of the chronic stenotic form of regional enteritis consists of either shortcircuiting the intestinal contents around the lesion, i e. ileocolostomy to the transverse colon, or of resecting the diseased bowel. If a resection is done, a long loop (20 to 30 centimeters) of normal bowel adjoining the lesion should be removed also so as not to leave behind any small focus of inflammation which might be overlooked on gross examination. Postoperatively such a small overlooked focus may progress and lead to a fresh stenosis of the bowel. This complication occurred in several cases reported in the literature. In our cases, resection of the involved bowel with a wide margin of normal intestine on either side of the lesion has given excellent results. Short circuiting operations reported by Brown, Barger, and Weber Cline, and others have given relief in about 50 per cent of the patients. In the other 50 per cent the pathological process progressed so that a resection of the involved bowel became necessary Since shortcircuiting operations are associated with less risk than a resection it may be that a two stage resection for cases of regional enteritis is the procedure of choice. If the symptoms disappear following the shortcircuiting, no further surgery is indicated. If however the symptoms persist or become progressively worse, resection becomes necessary

Regional enteritis complicated by persistent external intestinal fistula can be cured only by excision of the involved intestine and sinus tract. Attempted closure without resection usually fails. Crohn reports a case in which eight laparotomies were performed in a vain attempt to close an intestinal fistula following drainage of a right lower quadrant abscess. As soon as the pathological process was recognized to be a regional ileitis, the involved intestine was resected with the fistulous tract. Complete relief of symptoms and cure of the fistula followed.

Case 1 T F, aged 7 years, was first examined September 17 1933 The child was apparently well 3 days before examination After eating several hamburger sandwiches which had caused him no distress, his mother gave him a "prophylactic dose" of castor oil. The next day the child complained of diffuse abdominal pain and nausea. The pain became intermittent, cramp-like, and localized to the lower abdomen The following day the pain became more

Fig 1 The involved ileum appears as a stiff tube The serosa is dull, in places granular, and subserosal hemorrhages are present.

severe and colic like The cramps caused the patient to double up and cry The paroxysms of pain lasted for about 1 minute and subsided following which he was comfortable Upon admission to the hospital the cramp like pain recurred about every 4 to 5 minutes Vomiting occurred several times since the onset

Fig 2 Specimen in Figure 1 cut open longitudinally Note hyperplasia of the wall of the ileum, edema of the villous folds, and ulceration along the mesenteric side

Physical examination revealed a well nourished male child of about 7 years The temperature was 100 degrees F, pulse rate 98, and respiratory rate 18 Abdominal examination revealed tenderness in the right lower quadrant No masses were palpated Rectal examination showed no masses or pelvic tenderness The remaining physical examination was negative The white blood count was 12,000 A provisional diagnosis was made of an acute appendicitis

At operation the appendix was found to be grossly normal the terminal 10 centimeters of ileum was thickened and indurated, the serosa was injected The regional lymph glands were enlarged up to 3 centimeters and several were hemorrhagic The ileum proximal to the diseased portion was normal and not dilated A diagnosis was made of acute regional ileitis Believing that the pathological process would resolve spontaneously an appendectomy was done to simplify subsequent diagnosis and the abdomen closed

Following the operation the gastro-intestinal tract was examined roentgenologically every 2 to 4 months At first

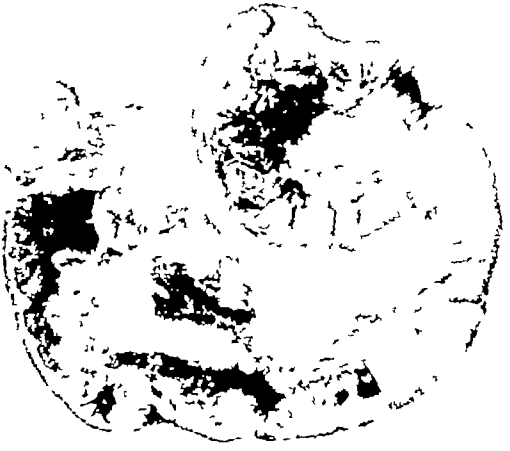

Fig 3 This resected specimen shows the wall of the terminal ileum thickened, the hyperplasia greatest at the ileocecal valve The head of the cecum is hyperplastic The mesentery of the ileum is thickened and contains a small abscess, which was walled-off by the adherent loop of ileum that is seen covered with fibrinous exudate in the proximal end of the resected specimen The lumen of the terminal ileum is narrowed, the narrowing is greatest at the ileocecal valve.

Fig 4 This specimen shows a more advanced stage of regional ileitis There is marked hyperplasia of the wall of the terminal ileum The wall of the cecum is thickened, particularly in the region of the ileocecal valve. The mesentery contains many sinuses which lead into the lumen of the terminal ileum The mucosa of the terminal ileum is granular and contains sessile and pedunculated polyps. Proximally, the mucosa is edematous, the villous folds are blunted and thickened The lumen of the terminal ileum is constricted and almost obliterated at the ileocecal valve

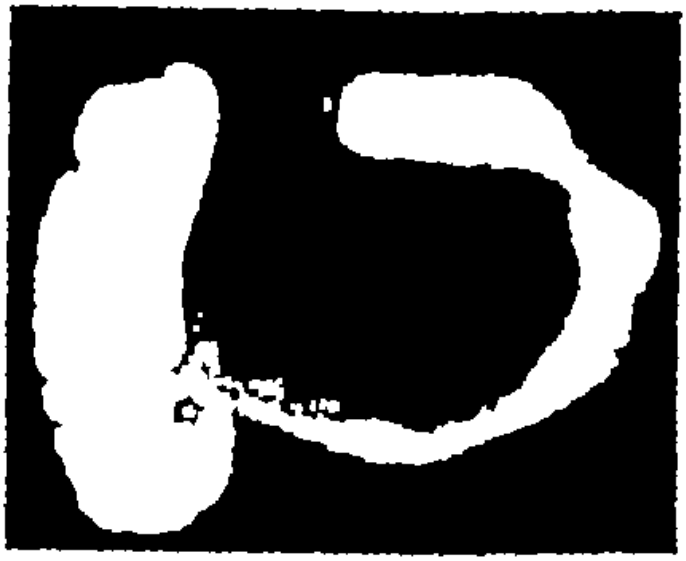

Fig. 3. Roentgenogram of specimen in Figure [illegible] injected with a watery solution of barium sulphate. The lumen of the ileum is uniformly narrowed. The constriction is more pronounced at the ileocecal valve and gradually diminishes proximally. In the distal portion of the ileum there are many sinuses which seem to have penetrated all the coats of the bowel wall to the subserosa. The cecum appears normal.

the last portion of the ileum was spastic so that it retained little or no barium for a distance of [illegible] to [illegible] centimeters. Subsequently the spasm was released and peristaltic waves could be seen traversing the entire involved ileum into the cecum. The last examination was on December [illegible], 1934, at which time the entire gastro-intestinal tract was normal. The patient had had no recurrence of her pain.

Case 2. Mrs. M. P., aged [illegible], was admitted to the Cook County Hospital on October 8, 1933. She complained that 6 hours before admission she noted the gradual onset of diffuse abdominal pain which at first was constant, dull, aching in character. Besides this constant distress the patient had periodic attacks of lower abdominal colic like pain, which could last for from [illegible] to [illegible] minutes and then gradually subside. The patient described these pains as similar to labor pains, although less severe. Nausea was present, but no vomiting occurred. There was no history of any previous similar attacks. The remaining general history was essentially negative.

Physical examination revealed a poorly nourished adult white female [illegible] years of age who appeared acutely ill. During the examination the patient would frequently double up when the colic like pain appeared, but after it had subsided, she was relatively comfortable. The temperature was [illegible] degrees F., pulse rate [illegible], respiratory rate, 8. Abdominal examination showed tenderness in the right lower quadrant. No mass was palpated. The remaining physical examination revealed nothing of apparent importance. The white blood count was 9,000. The urine was normal.

Since the symptomatology in this case was strikingly similar to that of Case [illegible], diagnosis was made of a regional ileitis. However an acute appendicitis could not be excluded. The patient was operated upon immediately. The appendix was grossly normal. The terminal 16 centimeters of the ileum was edematous and thickened. The ileum proximal to this area appeared normal. The regional lymph glands were enlarged. A diagnosis of acute regional ileitis was made. The appendix was removed to facilitate subsequent diagnosis and the abdomen was closed. The patient made an uneventful recovery. She was last seen November 4, 1934, at which time she was free from distress and roentgen examination of her gastro-intestinal tract revealed normal terminal ileum.

Case 3. Mr. T. R., aged 34, colored, was admitted to the Cook County Hospital July 26, 1934. He complained of general abdominal pain, fever, nausea and vomiting for about 36 hours. He was well until July 24, 1934, when at 2 o'clock in the morning he was awakened with a diffuse abdominal pain which was more intense in the right lower quadrant. The pain was colic like and radiated toward the right costal margin and at times to the left lower quadrant. The colics recurred every 3 to 4 minutes. The patient took a dose of magnesium sulphate, which he immediately vomited. The pain increased in severity. Shortly after the onset he had a watery bowel movement but worse were there. He had never had a previous similar attack. The remaining history disclosed nothing of apparent importance.

Physical examination revealed a fairly well nourished colored male aged 34 years. He had a temperature of [illegible] degrees F., pulse rate [illegible], and respiratory rate, 24. His abdomen was tender throughout, but most tender in the right lower quadrant. The peristaltic sounds were normal. There were no masses. The general physical examination was otherwise negative. He had a leucocytosis of 0,300.

A diagnosis was made of acute appendicitis. However at operation the appendix was grossly normal. The last 5 centimeters of the ileum was purplish red, edematous, and about one and one half times its normal size. The wall of the ileum was thickened and soggy. The lumen was narrowed. The involvement of the bowel was more pronounced at the ileocecal valve, diminished proximally and disappeared about [illegible] centimeters from the ileocecal valve. The mesentery of the involved ileum was injected, but not thickened. The regional lymph glands were not enlarged. The cecum and ascending colon appeared normal. The small bowel elsewhere appeared normal. An operative diagnosis was made of an acute regional enteritis of the terminal ileum. On account of the possibility of the spontaneous resolution of the inflammation of the ileum, an appendectomy was done to facilitate subsequent diagnosis, and the abdomen was closed.

The immediate postoperative course was uneventful, but approximately [illegible] hours after the operation had been performed the patient's temperature rose to [illegible] degrees F., pulse, [illegible] and respiratory rate, [illegible]. His skin was covered with cold perspiration. He remained in this condition for about 36 hours. He was given large quantities of saline solution by hypodermoclysis, but failed to improve. On the beginning of the third postoperative day he was given saline solution intravenously. Shortly after this his condition began to improve. About 3 weeks after operation the patient developed a pain in the right chest, which persisted about a week and subsided. A ray of the chest showed thickening of the pleura in the region of the right lower lobe and a moderate amount of fluid on the same side. There was no evidence of pulmonary tuberculosis. Subsequent roentgenograms of the chest showed the pathological process in the right base to be subsiding. Roentgen examination of the colon with a barium enema showed a normal colon. The ileocecal valve was competent. Examination of the terminal ileum following barium meal showed a normal terminal ileum. The patient was last seen March 10, 1935. He had had no recurrence of his abdominal distress and had gained about [illegible] pounds in weight.

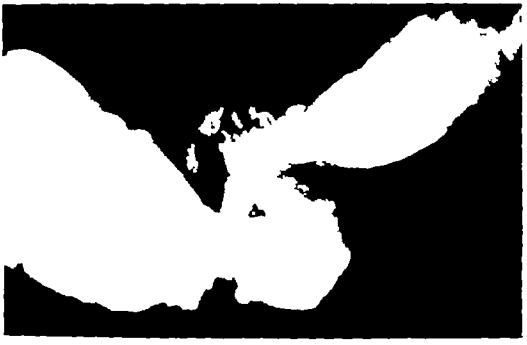

Fig 6 Roentgenogram of specimen in Figure 3 shows the barium filled sinuses penetrating through the wall of the ileum and leading into a common cavity which, at operation, was found to be mesenteric abscess

Fig 7 Roentgenogram of the specimen in Figure 4 There is a filling defect in the terminal ileum The lumen of the last portion of the ileum is narrowed The constriction is most marked at the ileocecal valve Along the mesenteric attachment there are five sinuses which extend from the lumen of the involved ileum into the mesentery where they meet in a common cavity from which barium seems to diffuse farther out in the mesentery Along the antimesenteric border the filling defect of the ileum is irregular and mottled This appearance is caused by the inflammatory polyps in this region Proximally there is a second constricted area along the mesenteric side of which two sinuses penetrate from the lumen into the mesentery The cecum is narrowed but its contour is smooth and regular

CASE 4[1] Mr H A, aged 20, first consulted us on January 4, 1933 For 2½ years he had had recurrent attacks of diffuse abdominal colic like pain This pain was sharp, paroxysmal, and seemed to be aggravated by eating There was no nausea, vomiting, or diarrhea Shortly after the onset of this illness he consulted a physician under whose treatment (non-residue diet and mineral oil) the symptoms disappeared for a year The pain then recurred It was more severe and tended to localize to the right lower quadrant. The pain remained colic-like in character, the colics lasted about 3 to 5 minutes and then tapered off to a dull constant ache or disappeared completely The abdomen became somewhat distended. There was no melena or diarrhea The patient lost about 20 pounds in weight during the last 2½ years His history otherwise contained nothing of apparent importance

Physical examination revealed a poorly nourished white male who did not appear acutely ill The temperature was 98 degrees F, pulse rate, 90, and respiratory rate, 20 Examination of the abdomen showed a moderate distention The peristaltic sounds were increased, but no peristaltic waves were seen A firm mass about 6 centimeters in diameter was palpated in the right lower quadrant The mass seemed immobile but was not tender The liver and spleen were not enlarged Physical examination was otherwise negative.

The erythrocyte count was 4,968,000, leucocyte count, 19,600, and hemoglobin, 80 per cent The blood Kahn and Wassermann reactions were negative

Roentgen examination of the gastro intestinal tract showed an annular "napkin ring" filling defect of the terminal ileum (Fig 14) Proximal to this constriction, the ileum was dilated The remaining gastro intestinal tract was roentgenologically normal The diagnosis made was "obstructive lesion of the terminal ileum"

The patient was operated on January 6, 1933 The abdominal cavity contained a small amount of serous fluid The terminal ileum was enlarged to about one and one half times its normal diameter It showed a hard edema The serosa was dull and covered by fibrinous exudate The process extended proximally from the ileocecal valve for about 25 centimeters and then gradually shaded off into normal ileum About 10 centimeters from the ileocecal valve there was an internal fistula between the diseased ileum and the middle of the transverse colon The mesentery of the terminal ileum was somewhat edematous The regional mesenteric lymph glands were enlarged The lesion appeared similar to the "terminal ileitis" described by Crohn and his co-workers We closed the opening in the transverse colon and resected about 35 centimeters of the colon and restored the continuity of the bowel by uniting the ileum to the transverse colon with a lateral anastomosis Following the operation he was given a transfusion of 500 cubic centimeters of whole blood The subsequent postoperative course was uneventful

The patient was examined last in January, 1935 He had gained about 40 pounds in weight and had experienced no recurrence of his abdominal distress Roentgen examination showed a normal colon, well functioning ileocolostomy and a normal ileum.

Pathological report The resected specimen consisted of the terminal 35 centimeters of the ileum, with cecum, appendix and ascending colon (Figs 1 and 2) The terminal 20 centimeters of the ileum was thickened and resembled a rubber hose in consistency On the serosa covering this portion of ileum there was some fibrinous exudate About 15 centimeters from the ileocecal valve along the mesenteric border of the ileum, there was a fistula which communicated with the lumen When opened, the lumen of the entire involved ileum was seen to be narrowed, the narrowing becoming more marked toward the ileocecal valve The bowel wall was thickened, measuring about 5 millimeters The lesion involved all the layers The mucosa was edematous, and along its mesenteric border there were many longitudinal ulcerations that in places seemed to extend through to the subserosa Roentgen examination of the specimen distended with a watery solution of barium sulphate (Fig 4) showed the narrowing more pronounced at the ileocecal valve and tapering off proximally In the terminal portion of the ileum there were many small sinuses which extended

[1] Cases 4 and 5 were previously reported in the Surg Clin of N Am, 1935 15 697

Fig 8 There is hyperplasia of the wall of the ileum, most marked in the muscularis and subserosa The mucosa is extensively ulcerated

Fig 9 Photomicrograph from specimen in Figure 3 Ulceration in terminal ileum extends through bowel wall into mesentery where it enters an abscess cavity

from the mucosa toward the mesentery Some of them seemed to penetrate through the muscularis to the subserosa The cecum appeared normal

Histological sections showed the wall of the ileum much thickened, partly by hypertrophy of the muscular layer and partly by an extensive inflammatory process that involved the submucosa and, to a greater degree, the muscularis and subserosa (Fig 8) This inflammatory infiltration consisted of nodular granulomas composed of hyaline connective tissue with many fibrocytes, histocytes and occasional giant cells (Fig 1) The granulomas were surrounded by accumulations of lymphocytes The giant cells were of the foreign body type In places, they seem to surround eosinophilic fibers (Fig 1) The mucosa was occasionally ulcerated The base of the ulcers was formed by recent subacute inflammatory tissue

Case 5 Mrs L B aged 32, was seen by us June 8, 1934 She complained of cramp like lower abdominal pain for about 7 weeks Her history was that 2½ months previously she delivered a full term child About 2 weeks following delivery she noted the gradual onset of cramp like lower abdominal pains The cramps would last up to minutes and then subside She consulted her obstetrician who discovered that she had a temperature of 99 to 100 degrees F daily and tender mass in the right tubo ovarian region On account of the recent childbirth and the above findings, a diagnosis of a puerperal infection was made. The patient was hospitalized and placed at bed rest for 3 weeks The abdominal cramps and fever persisted She left the hospital and remained in bed at home for several weeks with no relief of her symptoms The general history contained nothing of importance relative to her abdominal complaints

Physical examination revealed the abdomen somewhat distended Visible peristalsis was noted, particularly in the lower abdomen There were no areas of tenderness and no masses were palpated abdominally Pelvic examination disclosed an orange size, tender fixed mass in the right fornix The uterus was normal in size and position The left fornix appeared normal The remaining general physical examination revealed nothing of apparent importance The erythrocyte count was 4,040,000 leucocyte count, 8,700 and hemoglobin, 95 per cent Differential blood count showed neutrophils 8 per cent lymphocytes per cent, eosinophils 2 per cent, and monocytes, 4 per cent

Roentgen examination of the colon showed a filling defect in the head of the cecum Barium regurgitated into the ileum but the outline of the terminal ileum could not be seen clearly on account of the overlying sigmoid Examination of the ileocecal region after a barium meal disclosed narrowing of the last 2 centimeters of ileum Proximal to this constriction the bowel was slightly dilated (Fig 3) The head of the cecum showed the same filling defect noted with the barium enema The stomach and remaining small bowel were normal On account of the history of low grade fever for months with symptoms of partial intestinal obstruction due to an obstructive lesion of the terminal ileum, diagnosis of regional enteritis of the terminal ileum was made and resection advised

The patient was operated upon June 21, 1934 There was a small amount of serous fluid in the peritoneal cavity In the right fornix the mass that was previously palpated was a tumor involving the terminal ileum and the cecum The pelvic organs were normal The mass was not attached to the surrounding structures and was easily delivered from the abdomen The last 15 centimeters of ileum was thickened edematous, and boggy The serosa was covered with fibrin and was hyperemic The mesentery of the involved ileum was thickened and edematous A resection was done of the last 15 centimeters of the ileum, the cecum and ascending colon An ileocolostomy to the transverse colon was done with a lateral anastomosis After operation she was given a transfusion of 500 cubic centimeters of whole blood The remaining postoperative course was uneventful She last was seen May 1, 1935 At that time she was free from abdominal distress and had gained weight Barium enema showed a well functioning ileocolostomy and normal ileum

Pathological report The resected specimen (Fig 3) consisted of 36 centimeters of ileum with the attached cecum and colon The distal 7 centimeters of ileum was surrounded by a mass having a maximum diameter of 8 centimeters The serosa covering this portion of ileum was covered with fibrin The appendix which was incorporated in this mass was surrounded by fibrous tissue so as to form a cylindrical structure measuring 3 centimeters in diameter and located on the posterior surface Upon section, the tumor mass around the ileum was seen to be composed

Cases 4 and 5 were previously reported in the Surg Clin of N Am 1935, 15 997

Fig 10 An area in the subserosa shows infiltration by a non specific granulation tissue, which is surrounded by lymphocytes and lateral to it lies a foreign body giant cell

Fig 11 A higher magnification of a granuloma shows several giant cells which surround areas containing vegetable fibers

of fibrous tissue within which were islands of fatty tissue The lumen of the bowel was narrowed to 3 millimeters in the narrowest diameter, and 8 millimeters in the widest portion The mucosa was granular and projecting from its surface were several pedunculated polypoid masses measuring up to 1 centimeter in length The entire cecum was shrunken, its wall thickened, the mucosa roughly granular injected, but not ulcerated The thickening of the cecal wall was chiefly due to an increase in the submucosa This thickening gradually diminished in passing to the ascending colon, which was grossly normal The mesentery of the ileum was greatly thickened and indurated, increasing to 4 centimeters at the ileocecal valve Within the mesentery sinus tracts were easily followed into the lumen of the ileum, and connected with one another The proximal ileum exhibited a moderate thickening of the muscular coat (hypertrophy) with dilatation of the lumen to as much as 3 5 centimeters in diameter The histological findings in this case were the same as in Case 4

Injection of the specimen with barium sulphate (Fig 7) showed a filling defect of the cecum which corresponded essentially to the filling defect seen in the roentgenogram before operation The terminal ileum was narrowed Along the mesenteric border, 5 sinus tracts were followed from the lumen into the mesentery where they converged to a central irregular mass of barium (abscess cavity) Proximally, in the ileum there was a second narrow portion at which point two small sinus tracts extended from the bowel into the mesentery There was a filling defect on the antimesenteric surface in this area The remaining ileum and colon appeared normal in contour

CASE 6 Mrs F P, aged 25, was referred to us by Dr Charles Pugh, on June 1, 1934 She complained that 2 days prior to admission she noted the gradual onset of a bloating and abdominal distention She had no desire for food About 24 hours after the onset she experienced a sudden sharp pain in the right lower quadrant of the abdomen The pain lasted about 5 minutes and was later followed by continuous pain in this region The sharp colic like pain occurred about every hour and was severe enough to awaken her from sleep There was no nausea or vomiting The remaining history disclosed nothing of apparent importance

Physical examination at the time of admission to the hospital showed the patient fairly well nourished and not acutely ill She had a temperature of 100 degrees F, pulse rate, 90, respiratory rate, 18 Examination of the abdomen disclosed tenderness in the right lower quadrant No other abnormal signs were noted The general physical examination was essentially negative The white blood count was 11 000 On account of the indefinite abdominal pain and tenderness localized over the appendix, with a leucocytosis, a diagnosis of acute appendicitis was made The patient was operated upon immediately The ileum was found enlarged to about one and one half times its normal size, its walls were edematous and soggy The mesentery of the involved ileum was thickened to about 1 5 centimeters The cecum and appendix appeared normal The pathological process grossly was that of a regional enteritis of the terminal ileum On account of the possibility of spontaneous resolution, we removed the appendix to facilitate subsequent diagnosis, and closed the abdomen The postoperative course was uneventful She was discharged from the hospital on the tenth postoperative day Shortly after the patient was home she developed a dull, continuous pain in the right lower quadrant with paroxysms of abdominal cramps About 1 month after operation she developed recurrent paroxysms of severe pain in the right lower quadrant associated with a temperature of 103 degrees F The pain and fever lasted for about 13 hours and gradually subsided These acute attacks occurred about every 4 to 7 days No nausea or vomiting was noted There was no diarrhea or melena The patient gradually lost weight Roentgen examination of the ileocecal region following a barium meal on two occasions during the postoperative period showed transitory spasm of the terminal 4 to 6 centimeters of the ileum. No constant filling defect was demonstrated The ileum proximal to the spastic portion was slightly dilated Barium enema showed no pathology in the colon The cecum showed slight narrowing in the region of the ileocecal valve Barium regurgitated into the ileum which in its last 2 centimeters showed a filling defect, whereas, the bowel proximal to this point appeared normal On account of the recurrent pain and fever, and the filling defect in the terminal ileum, a diagnosis was made of a stenotic type of regional enteritis

The patient was re-operated upon on July 5, 1934. There was a small amount of serous fluid in the peritoneal cavity The disease in the terminal ileum was more extensive than at the first operation A loop of ileum was adherent by fibrinous exudate to the mesentery of the terminal ileum Upon separating this loop of ileum from the mesentery, a small abscess cavity was opened The last two feet of the ileum, cecum, and ascending colon were resected and a side-

Fig. 3. A barium enema shows the cecum uniformly constricted in the region of the ileocecal valve. The remaining colon is normal.

to-side anastomosis was done between the ileum and transverse colon. After operation she was given a transfusion of 500 cubic centimeters of whole blood. The remaining postoperative course was uneventful. She was last seen May 1935, at which time she had gained 10 pounds in weight and her abdominal symptoms had disappeared.

Pathological report. The specimen (Fig. 4) consists of 30 centimeters of the ileum with the cecum and ascending colon. The mesentery at the ileocecal angle is thickened to about 3 centimeters and appears as a firm mass, 8 by 8 centimeters, partially encircling the bowel. Within this mass there is an abscess 1 centimeter in diameter. In the proximal portion of the resected ileum the bowel is surrounded by fibrinous exudate which forms one of the walls of the above mentioned mesenteric abscess. The lumen of the distal 2 centimeters of ileum is narrowed to 6 millimeters in diameter, where the lumen is of normal size. The wall of the terminal 8 centimeters of the ileum is thickened to 5 millimeters. The hypertrophy involves all the layers. The mucosa is edematous and the villous folds are thickened. Linear ulcers of the mucosa are present along the mesenteric attachment of the last 3 centimeters of the ileum. The wall of the cecum in the region of the ileocecal valve is thickened to 4 millimeters. The mucosa in this portion of ileum is edematous, but contains no ulcers.

The macroscopic findings were essentially similar to those described in Case 4. A section taken through the ileum including the ileocecal valve (Fig. 9) showed ulceration of the mucosa penetrating through the bowel wall and leading into an abscess cavity in the mesentery.

Injection of the specimen with barium sulphate showed a filling defect in the terminal ileum involving the ileocecal valve (Fig. 4). On the mesenteric side of the filling defect small sinus tracts are seen extending out from the bowel to the mesentery. Here they coalesce into a large irregular mass of barium which corresponds to the walled-off mesenteric abscess noted during the operation.

Case 7. Mrs. C. U., aged 27 years, was first examined September 2, 1930. For the past 3 years she had recurrent attacks of cramp-like periumbilical pain which occurred during and after meals. The pain was often associated with diarrhea. There was no nausea or vomiting. Her last attack began 1 week prior to our first examination at which time she experienced severe paroxysmal lower abdominal cramp-like pain which was accompanied by vomiting. No diarrhea was present with this attack. There was no vomiting until the last attack. The past history relative to the present illness was that when aged 11 years the patient had an abdominal complaint which continued for about 1 year. The pain at that time was periumbilical and occurred during and after meals. She was free from distress until 18 years of age when an appendectomy was performed for this indefinite abdominal distress. Following the operation she remained well until the onset of her present illness 3 years ago.

Physical examination revealed a poorly nourished adult white female who did not appear acutely ill. The temperature was 98 degrees F., pulse rate, 80, respiratory rate, 18. Abdominal examination showed an appendectomy scar, diffuse lower abdominal tenderness and slight distention. No masses were found on abdominal palpation, but pelvic examination revealed a tumor mass in the right adnexal region. The remaining physical examination was negative. The diagnosis made was a pelvic tumor.

The patient was operated September 23, 1930. The small intestines in the lower abdomen and pelvis were matted together by fibrinous adhesions. While separating the loops of bowel, an abscess was opened into. Several drains were placed into the abscess cavity and the abdomen closed without further exploration. Subsequent to the operation the patient developed fecal fistula which persisted up to the time she was discharged from the hospital, October 27, 1930.

The patient remained under observation for about a year, during which time the fistula resisted all types of non-surgical treatment. On account of the failure to close, resection of the fistula was advised.

At operation the fistulous tract led to the terminal portion of the ileum, which was thickened and edematous. The last 20 centimeters of ileum was resected, and the continuity of the gut restored by a lateral anastomosis between the ileum and the cecum. The patient made an uneventful recovery. She was last seen November 5, 1931, when she was free from abdominal complaint.

We regret that the specimen and histological sections of this case have been lost. However, at the time of operation the resected bowel was found thickened and the mucosa was ulcerated along the mesenteric border. The appearance macroscopically was that of a regional ileitis.

Case 8. Mrs. C. P., aged 3 years, was admitted to the Cook County Hospital October 17, 1931. She complained that about 3 weeks prior to her admission to the hospital she experienced the gradual onset of cramp-like lower abdominal pain associated with nausea and vomiting. Abdominal distention became noticeable. Vomiting, which at first was bile stained, later became fecaloid. Constipation was noted although the patient had slight bowel movements with enemas. The past history was apparently negative except for an attack of pain in the left kidney region associated with dysuria and frequency about 3 months previously. She was treated at that time in another hospital for pyelitis.

Fig. 13. Roentgenogram taken after a barium meal shows the terminal ileum narrow and irregular in outline and lies in the form of a letter U. There is a filling defect in the head of the cecum.

Fig. 14. In this roentgenogram taken after a barium meal a constriction or a "napkin ring" filling defect of the terminal ileum with dilatation of the ileum proximal to the defect is demonstrated.

Physical examination showed a well nourished white woman who appeared acutely ill. The temperature was 103 degrees F., pulse rate 90, and respiratory rate 20. Abdominal examination showed a moderate distention particularly over the lower abdomen. There was visible peristalsis which was associated with an increase in the peristaltic sounds (borborygmi). There was diffuse tenderness over the lower abdomen, particularly on the left side. The general physical examination revealed nothing of apparent importance. The white blood count was 18,500. A diagnosis was made of subacute small intestinal obstruction.

The patient was operated upon October 18, 1933. An orange sized mass was found in the lower abdomen. The mass consisted of loops of small bowel and omentum which were adherent by fibrin. Several loops of small bowel were dilated to about 5 centimeters in diameter, whereas others were about 2 centimeters in diameter. The dilatation of the bowel appeared to stop about [illegible] meters from the ileocecal valve. The wall of the dilated bowel was edematous, thickened, and measured about 5 millimeters in thickness and appeared subacutely inflamed. Upon separating the loops of intestine and omentum that comprised the mass an area of constriction was found about 1 centimeter long which seemed practically completely to obstruct the lumen. There was fistulous communication between a loop of unobstructed small bowel and the dilated intestine just proximal to the site of obstruction. A V type of resection of the obstructed area, including the fistulous opening, was performed without cutting the mesentery. The bowel was reunited by an end to end anastomosis. After operation the patient was given a transfusion of 500 cubic centimeters of whole blood. Her subsequent course, except for a wound infection, was uneventful.

Histological examination of the excised pieces of bowel showed a marked thickening of the bowel with chronic inflammatory granulation tissue, non specific in nature.

SUMMARY

Eight cases of regional enteritis, one of the jejunum and 7 of the ileum, are reported.

Four of the patients had acute regional enteritis. In 3 the process resolved spontaneously and in 1 it progressed to the chronic stenotic phase.

There were 4 cases with the chronic stenotic type of regional enteritis. Two had lesions of the terminal ileum. One patient who had a lesion of the terminal ileum complicated by a large abscess and developed following drainage of the abscess a persistent external intestinal fistula which required resection. The fourth case had a regional jejunitis.

The pathological anatomy is that of a non-specific inflammation. The acute regional enteritis consists of an infiltration of the bowel wall by an acute inflammatory granulation tissue with

extensive ulceration of the mucosa. This process may resolve spontaneously or progress to the chronic phase. The chronic forms of regional enteritis are usually associated with a hyperplasia of the intestinal wall by a non-specific inflammatory granulation tissue which contains granulomas, foreign body giant cells, and an excessive amount of connective tissue. Linear ulcers of the mucosa are present along the mesenteric border of the bowel. In the terminal ileum these ulcers penetrate through the bowel wall and form sinuses that lead into the mesentery which is frequently the site of an abscess. Internal and external intestinal fistulas may develop and lead from the involved intestine to an adherent loop of bowel or abdominal wall. The pathogenesis of this regional inflammation of the intestines is not known. Clinical and pathological studies have failed to demonstrate any evidence of tuberculosis, actinomycosis, syphilis, or Hodgkin's disease.

The symptomatology of regional enteritis varies with the different phases of the pathological process and with the location of the lesion. The symptoms in the acute types of regional enteritis, particularly of the ileum, usually simulate an acute appendicitis. The symptoms in the chronic forms mimic a low-grade intestinal obstruction or ulcerative colitis. Persistent external intestinal fistulas develop following drainage of an intra-abdominal abscess which is a sequel of the regional enteritis. The lesions higher in the intestinal tract tend to give symptoms of an intestinal obstruction more frequently and more rapidly than lesions in the ileum or colon. The diagnosis in the acute types of regional enteritis is usually made at operation undertaken for an acute appendicitis or an acute surgical abdomen. In our series of cases the symptoms in the patients with an acute regional enteritis were those of an acute incomplete intestinal obstruction. The physical findings corresponded closely to those of an acute appendicitis. This association of symptoms and physical signs of acute intestinal obstruction and acute appendicitis may be an aid in establishing the diagnosis of an acute regional enteritis. The diagnosis of chronic types with stenosis of the bowel is usually made by roentgen examination which shows a filling defect in the involved intestine.

The treatment of regional enteritis varies with the phase of the pathological process. Acute regional enteritis limited to the bowel and not associated with thickening of the mesentery may resolve spontaneously. If, however, the mesentery is thickened and indurated, it is probable that ulceration of the mucosa has extended into the mesentery; spontaneous resolution then is less likely to occur and a shortcircuiting operation or a resection is indicated. Chronic regional enteritis with stenosis is best treated by resection or a shortcircuiting operation. When complicated by an external intestinal fistula, resection of the involved bowel with the fistulous tract is necessary to close the fistula.

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THE TREATMENT OF ABORTION

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THE accidental or criminal termination of a pregnancy in its early months results in a condition which frequently offers a serious problem in treatment. Nor is it uncommon for an ethical physician to be called upon to administer to a patient upon whom a criminal abortion has been attempted or partially completed. When such a situation arises, it becomes his duty to treat such a patient and do whatever may be possible to spare her. If the abortion should be accidental, he must likewise be prepared to handle the case in the most rational manner. Many factors may arise in the individual case which make it necessary to exercise extreme judgment in its management. It would seem that the importance of selecting the proper procedure in these cases has been emphasized too little. Obviously no definite steps may be set forth which can be applied to all cases, but certain definite principles have been accepted, more or less, which may be applied to the advantage of the patient. It seems appropriate, therefore, to present a study of the various types of abortion which have been observed at Cleveland City Hospital, the method of management, and the results obtained by such treatment.

This study represents a total of 445 cases which were observed at Cleveland City Hospital during the 2½ years from July 1, 1932, to January 1, 1935. A more or less uniform practice in the treatment of the fairly large series of cases, which were seen during this interval, affords an excellent opportunity for appraisal of results. No therapeutic abortions or threatened abortions are included. In a number of instances, the differential diagnosis presented some difficulty, but no cases are included in which the diagnosis of abortion was not proved by definite clinical evidence or positive pathological findings. In several cases a definite diagnosis was not established before postmortem examination. It is reasonable to suppose that many of the abortions were accidental or spontaneous, but it probably would be conservative to estimate that 70 per cent or more were induced by some sort of intrauterine manipulation. Because of the unreliability of histories obtained, no exact figures concerning this are presented. That there should be great variation among the individual cases of such a series is obvious. In fact, when viewed from a distance, the whole series represents a rather bizarre aggregate from which to draw any convincing conclusions, but certain constituents appear in the study which are worth noting.

CLASSIFICATION OF CASES

Any termination of pregnancy before the end of the twenty-eighth week of gestation is classified as an abortion and is included in this series. If the abortion took place the first 16 weeks of the pregnancy, it is spoken of as an *early abortion*; if it occurred between the sixteenth and twenty-ninth weeks, it is termed *late abortion*.

Incomplete abortions. Any case in which reasonable evidence could be obtained to show that part of the products of conception had been expelled before admission, fits into this group. These constitute by far the largest group in the series with a total of 325 cases, 275 of which were early and 50 late.

Complete abortions. This group is represented by those cases in which the contents of the uterus have been completely expelled before admission, as proved by exploration of the uterus or substantial clinical evidence. Occasionally these patients are grossly infected, but most in this series provided no serious problem of treatment. There were a total of 50 cases, of which 40 were early and 10 late.

Inevitable abortion. An abortion is classified as *inevitable* when none of the products of the pregnancy have been expelled before admission, but in which instance the pregnancy is terminated during the hospital stay. Here, there arises the added responsibility of preserving the pregnancy if such is possible without endangering the health of the mother too greatly. In all, 70 such cases were observed. Of these, 41 were early and 29 late. Spontaneous completion took place in 20 of the early cases and 18 of the late cases, while in 21 of the early cases and in 11 of the late cases operative completion was required.

TREATMENT

Needless to say, much controversy exists regarding the treatment of the patient who presents herself with evidence to indicate that an abortion is pending or in progress. Many factors are to be considered, but the outstanding point of discussion is whether or not the uterus should

be invaded and the abortion completed when evidences of uterine infection are present. Much has been said against any such operative intervention when active infection is present. There are those who maintain that in the presence of fever and/or malodorous discharge, conservative measures of a supportive and palliative nature should be followed strictly However when the various types of cases are considered, it will be seen that to empty the uterus without too much delay will possibly be of great benefit in certain cases. Foremost of these are those instances in which hemorrhage may be so profuse as to be an immediate danger to the life of the patient. This usually occurs when the products of conception are separated from the wall of the uterus but not expelled from its cavity To remove this material allows the uterus to contract and the bleeding ceases. It is notable, also, that many patients entirely fail to respond to palliative measures. In these, it becomes obvious that the presence of the necrotic infected material in the uterus, from which absorption is continually taking place, is working to the detriment of the patient. Often removal of this necrotic tissue results in a spectacular crisis and a rapid return to normal. From an economical standpoint, to empty the uterus at the earliest time when it may be considered safe, considerably shortens the patient's hospital stay

Although it may be desirable to complete an inevitable or incomplete abortion as soon as possible It must be kept in mind that to invade the uterus in the face of active infection is not without certain danger to the patient, as will be shown later It is probable that in certain situations, this added risk is justifiable. Also it will be pointed out that there is most likely an optimal time to complete the abortion even after the infection has subsided. It is rightly emphasized that when an infected uterus is subjected to the trauma of operative procedure, the so called "leucocytic barrier" is broken down and a spread of the infection made probable. Likely the danger of such is greater when the invading organism is the hemolytic streptococcus.

General procedure At Cleveland City Hospital, during the interval covered by this study, the general treatment of these cases has been fairly uniform. Often the patients admitted are in serious condition, many being severely exsanguinated, extremely toxic, or even moribund. First attention is always directed to supporting the patient generally Fluids are given in whatever way may be possible. If anemia is marked, preparations are made for transfusion. Usually unless it is thought that the abortion is only threatening, oxytocics are administered at once. These tend to check bleeding and probably lessen "toxic" absorption. As a rule the patient is given every opportunity to complete the abortion spontaneously When the uterus has contracted firmly gentle but firm suprapubic pressure may serve to express the secundines completely If this is unsuccessful, it is preferred to do no more to the patient for 24 to 48 hours.

TABLE I.—SUMMARY SHOWING MANAGEMENT OF 445 CASES

	Cases
Abortion at time of admission	98
Spontaneous or non-operative completion after admission	107
Operative completion	
Dilatation of cervix and curettement.	93
Dilatation of cervix and removal of tissue, only	40
Curettement, without dilatation of cervix	54
Removal of tissue without dilatation or curettement	85
Died with abortion incomplete	16

Afebrile abortions If not complicated by serious blood loss, these cases are easily managed. Often the abortion is spontaneously completed within 48 hours. If such is not the case, the uterus is emptied by the least traumatizing procedure. Usually this can be done without further dilating the cervix and without using the sharp curette. Our experience has shown that this can be done without being followed by serious morbidity

Infected abortions. These may include any case, from that showing a slight elevation of temperature and few constitutional symptoms, to the acutely ill patient with chills and fever or slight fever and an extreme degree of prostration. When first seen, it is usually impossible to predict the ultimate course of the process but it is noteworthy that the patient who shows slight or no fever low blood pressure which cannot be explained by blood loss, feeble pulse and extreme prostration, almost always responds poorly to all therapy It can strongly be suspected that this patient harbors an infection of virulent streptococci, and all intra-uterine manipulation positively should be avoided. Less concern should be felt for the patient who shows high fever chills, full bounding pulse, and who does not appear so ill. Here it probably may be considered that the uterus is invaded by the usual saprophytic organisms.

The infected case is generally treated "conservatively" If hemorrhage is not severe and the patient responds satisfactorily to palliative measures, time is allowed for the temperature to sub-

side. Frequent small transfusions of whole blood have proved excellent supportive treatment in patients with severe infection When the fever has been lower than 100 4 degrees F for 24 to 48 hours and it is felt that the uterus is not empty, operative completion is done

TABLE II —TIME OF SURGICAL INTERVENTION

Time of Intervention	Cases
Within 24 hours of admission	
Febrile	15
Afebrile	63
During febrile stage after 24 hours observation	47
Afebrile 24 hours	57
Afebrile 48 hours	38
Afebrile 72 hours or longer	49

Occasionally that case is seen in which it is felt advisable to empty the uterus in spite of an existing febrile state Not infrequently the response is favorable, but it must be heeded that such a step definitely increases the patient's chance for morbidity, which may be serious It must not be undertaken unless it is felt that the patient's general condition warrants such a risk It will be seen in Table II that this was a not infrequent procedure in this series, but our morbidity rate in these cases is tending to result in fewer patients being handled in such a manner (Fig 1)

Inevitable abortion These cases are peculiar only in that an effort should be made to save the pregnancy, if possible If active infection is present, treatment is as for other infected abortions, and oxytocics are given without regard for the pregnancy If afebrile and the Friedman test indicates that the fetus is dead, the uterus is emptied without delay Otherwise, the abortion is treated as *threatened*

TREATMENT OF COMPLICATIONS

Treatment of the complications of abortion is necessarily highly individualized However, some general observations as to the manner with which these are dealt, as they arise, would be in order

Hemorrhage Profuse bleeding, even to the point of exsanguination, is a common complication of abortion, and must at times be dealt with immediately Temporary support of the circulation by means of intravenous infusions of normal saline solution, to which epinephrine may be added, is sometimes of great benefit. Solutions of isotonic glucose, or gum acacia, are administered in the more severe cases in order to support the patient while preparations are being made for blood transfusion Blood transfusion was

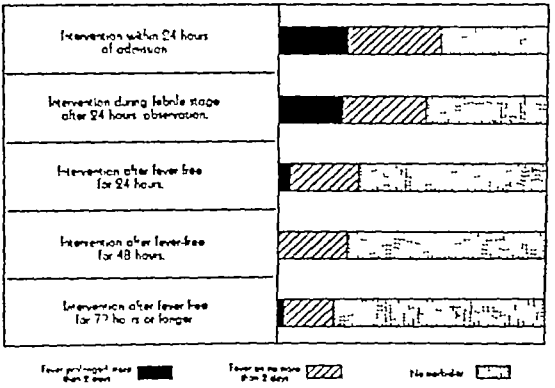

Fig 1 Illustrating the extent of the morbidity following operative treatment, with relation to the febrile state of the patient at the time at which the operation was done.

used freely in this series As soon as a satisfactory donor can be secured and preparations completed, the patient is given 500 cubic centimeters of whole blood by the Vincent tube method No serious reactions to transfusion were noted, and many patients were undoubtedly greatly improved by the procedure Transfusion is usually considered indicated when the red blood cell count is below 3,000,000 per cubic millimeters, or when the patient shows signs of shock due to blood loss

The hemorrhage occasionally necessitates early interference in these cases because of its severity The usual methods to control hemorrhage are used, consisting of shock position, application of external heat to the extremities, ice bag to the fundus uteri, and the administration of ergot, pituitrin, and more recently pitocin If bleeding continues in spite of these measures and the abortion does not complete itself within a few hours, the uterus is emptied, care being taken to cause as little trauma as possible When done gently, this procedure should carry with it very little morbidity Often it is not even necessary to administer a general anesthetic

Sapremia The less virulent infections, associated with abortion, have previously been considered to be "sapremic," and were thought to be brought about by putrefactive bacteria A copious, malodorous discharge was thought to be characteristic of this condition which was formerly looked upon as an entity Observations in this series would lead us to believe that the character of the discharge, *per se*, as well as the presence or absence of chills, does not differentiate between a relatively benign infection and one of more serious import. However, as pre-

viously stated, the patient with high fever but not appearing very ill, has usually proved to have a mild type of infection. These patients are treated by bed rest in Fowler's position, application of heat to the lower abdomen, and the administration of oxytocics.

Septicemia. This unfortunate complication explained the death in a high percentage of the cases which terminated fatally. General supportive measures, fluids, and frequent small transfusions of whole blood, seem to be of the greatest benefit in such cases. Continuous intravenous drip has proved to be a valuable technique in the administration of saline and glucose solutions. In some instances "strepto-lysate" or "colo-lysate" were employed with some apparent benefit.

Endometritis. It is well known that there is considerable inflammation of the endometrium in all abortions whether they be criminal in origin or otherwise. Two very marked cases of endometritis were associated with placenta accreta. Endometritis is more commonly a preliminary infection, usually relatively mild, but occasionally is followed by other evidences of pelvic infection. It is very probable that all cases of "sapremia" are really examples of endometritis plus the presence of infected products of conception. The treatment is that recommended for sapremia.

Parametritis, pelvic cellulitis and *pelvic peritonitis.* These are dealt with by giving the patient complete rest in bed, mild catharsis, abundant fluids, Fowler's position, and moist heat to the lower abdomen. The Elliott technique for administering pelvic heat is of outstanding benefit in these cases, frequently causing rapid resolution of the process, or aiding in the localization of an abscess.

Pelvic abscess. This was encountered occasionally in this series. Treatment is palliative until the abscess localizes and may be drained. Posterior colpotomy is the method of choice if the abscess is accessible by this route. Abscesses of the broad ligament are treated by Cullen's method of retroperitoneal drainage, unless pointing to the midline where they may be reached by pelvic puncture. In a few such cases dramatic results were obtained by posterior colpotomy when only a small abscess was evacuated.

Phlebitis. Elliott treatment and hot douches are found to be efficacious in cases of pelvic phlebitis. Phlebitis, or thrombophlebitis, of the femoral or saphenous veins is treated by elevation of the extremity under an electrically heated cradle. Prolonged bed rest is important in any case, together with support of the peripheral venous circulation by means of proper bandages or stockings when the patient is allowed out of bed. Hysterectomy is not done for pelvic phlebitis, and conservative measures are employed at all times. No instances of pulmonary embolus could be shown in the entire series.

TABLE III.—MORBIDITY OF OPERATIVE CASES

Reaction	Cases	Per cent
Febrile before completion, no morbidity after	106	39.4
Febrile before completion morbidity after	5	1.8
Afebrile before completion, morbidity after	13	4.8
Afebrile; no morbidity	99	36.4
Died after operative completion	3	1.0
Total number operative cases	272	

MORBIDITY AND MORTALITY

A careful study of the morbidity and mortality in this group of cases furnishes the best denominator by which to evaluate the results of the method of treatment followed at Cleveland City Hospital. In order to measure such a variable as morbidity certain arbitrary points must be accepted. Our term "morbidity" is taken as that suggested by Stander[1] to apply to the puerperium. A case is spoken of as having had "morbidity" when there has been a temperature rise of 100.4 degrees F., or more, on any two 24 hour periods following operation, excluding the first 24 post operative hours or when the temperature has remained elevated longer than 24 hours. The term "febrile" will be used to indicate the presence of a temperature of 100.4 degrees F or more, but not in the same restricted sense as "morbidity."

Total morbidity. Of the 445 cases studied, 254 cases, or 57 per cent, were febrile at some time during observation. This does not include the small number of patients who showed a slight febrile reaction, after operation, but no morbidity. Among the 50 patients admitted as complete abortions 24, or 48 per cent, were febrile. Of those who completed spontaneously or merely with the aid of suprapubic pressure, 54, or 50.5 per cent, of the 107 cases were febrile. Table III shows the morbidity in the cases that were treated by some operative procedure. It will be seen that the morbidity and febrile reactions compare favorably with the group percentage.

Morbidity of operative cases. It is demonstrated in Table III that those patients who were afebrile before operation had very slight tem

[1] Stander, H. J. Am. J. Obst. & Gynec., 1924, 8: 471.

perature reaction to the treatment In a large number of patients who had fever before intervention there was no subsequent morbidity Aside from 3 cases with fatal termination there was a total morbidity after operation of 23 6 per cent, which must be accepted as a relatively low figure Obviously the morbidity and mortality were low in the operative cases because those patients who were in critical condition were rarely subjected to intra-uterine manipulation However, it may further be pointed out that when done in properly selected cases, the danger from operative completion of abortion is relatively slight

Morbidity and type of operative procedure The morbidity following operative completion of an abortion appears to bear some direct relation to the manner in which the uterus was emptied

Table IV illustrates the percentage of cases showing morbidity following various types of operative completion of abortion It is noted that this is morbidity seen in patients who were afebrile for at least 24 hours before operation It is outstanding that those cases in which the least was done showed the lowest morbidity in spite of the fact that these were most often the recently infected cases When the uterus was emptied without dilating the cervix and without using a curette, the morbidity was only 3 5 per cent. Dilatation of the cervix and curettement of the uterine wall gave a morbidity of 7 7 per cent. A notable point in this study is that dilating the cervix carries with it a higher morbidity than gently curetting the uterus It is not difficult to conceive the greater trauma associated with any method of forcible dilatation of the cervix In spite of the small number of cases presented, it must be concluded that all unnecessary trauma and manipulation should be carefully avoided when invading the infected or potentially infected uterus Even vigorous bimanual examination under anesthesia must be looked upon as capable of causing dangerous dissemination of the disease process

Relation of morbidity to the time of surgical intervention From our study, it would appear that the time at which an operative completion is done bears no little importance to the morbidity rate Figure I shows the time, with relation to the febrile state of the patient, at which the completion was done and the resulting reaction These cases were grouped according to those which showed no more than a temperature rise of 100 4 degrees F or above on 2 postoperative days, excluding the first 24 postoperative hours, those which showed a temperature reaction more

TABLE IV —MORBIDITY AND TYPE OF SURGICAL COMPLETION

Procedure	No	Morbid	Per cent Morbidity[1]
Dilatation of cervix and curettement	91	7	7 7
Dilatation of cervix and removal of tissue, only	40	4	10
Curettement, without dilatation of cervix	54	3	5 5
Removal of tissue, without dilatation or curettement.	84	3	3 5

[1] Patients were afebrile for at least 24 hours before operation.

extended than this, and those which showed less than the minimal reaction The latter group were conceded to be without morbidity. It will be seen that the temperature reaction was greater and more often prolonged when operation was done while the patient was febrile The high morbidity among those patients who had surgical intervention within 24 hours of admission may be explained by the fact that they had been observed too short a time to determine the presence of active infection Consequently, a number of patients were operated upon who would not have been included had they been observed a longer time Also, many of these abortions were completed because profuse bleeding made it imperative The results of this study confirm our opinion that the optimal time to complete an abortion, if at all, is when the patient has been afebrile for 48 to 72 hours Nothing is to be gained, usually, by delaying longer, and to invade the uterus earlier carries a greater risk for the patient.

Accidents of treatment Perforation of the uterus occurred in only 1 case of those 272 which received surgical completion In this case the posterior wall of the uterus was perforated with the Hegar dilator and omentum was delivered through the opening The abdomen was not explored and recovery was uneventful Patient was discharged after 14 hospital days

Mortality In this series there were 21 deaths, or a gross mortality of 4 72 per cent. This mortality is really low, when the type of case handled at City Hospital is considered It is notable that many of these patients were moribund at the time of admission and that 7, or one-third, of the deaths occurred within 24 hours of the time the patient was admitted The average number of hospital days for the fatal cases was 7 9, although 1 case was in the hospital 44 days It is interesting to observe that in 12 of these patients, there was an admitted history of criminal attempt to induce the abortion, and in 1 other case there was postmortem evidence to

indicate that the uterus had been perforated before admission to the hospital. Only 3 deaths occurred following operative treatment in City Hospital. These are worthy of individual mention. In 1 there was a history of criminal abortion by means of packing the cervix with cotton on two occasions. On admission the patient was bleeding profusely had high fever and chills, and appeared quite ill. A transfusion and dilatation and curettement were done immediately. Following operation the patient continued to become worse, developed a cellulitis of the buttocks, and died after 21 hospital days. There was no post mortem examination. In a second case, death occurred on the operating table after 7 minutes of nitrous oxide gas anesthesia. No postmortem examination was permitted. The third death resulted from profuse uterine hemorrhage some hours after the patient had been transfused and the uterus apparently emptied. Hemorrhage was profuse and sudden and there was no time to complete a second transfusion.

SUMMARY AND CONCLUSIONS

1. A study of 445 cases of abortion observed at Cleveland City Hospital during a period of 2½ years is presented. Over this interval the method of treatment was fairly uniform and affords suitable opportunity for appraisal of results.

2. The general tendency in treatment is toward a policy of non-intervention. It is recognized that invasion of the uterus, especially in the face of active or potential infection, may be exceedingly hazardous. However it is believed that circumstances justify this risk in some instances.

3. The importance of blood transfusion as a life-saving measure in extreme exsanguination and as a therapeutic procedure in the presence of infection is properly stressed.

4. Intra uterine manipulation is avoided in all cases if practical. Opportunity is allowed for spontaneous completion unless hemorrhage is severe or other conditions warrant immediate intervention. However if the abortion is still incomplete after the patient has been afebrile for 48 hours, it is thought that there is no advantage in delaying completion for a longer time.

5. Of the 445 cases observed, 272 were treated by some type of operative evacuation of the uterus. It is shown that the optimal time to empty the uterus, when infection has been present, is after the temperature has been below 100.4 degrees F for 48 hours. It is important to carry out this procedure with a minimum of trauma, avoiding dilatation of the cervix and curettement if possible. When the uterus is emptied at the proper time in properly selected cases and with minimal trauma, the morbidity following operative procedures is not excessive and is of a benign nature.

6. This series presents a total of 21 deaths—a gross mortality of 4.72 per cent. One-third of these deaths occurred within 24 hours of the patients' admission to the hospital. Only 3 followed operative treatment at City Hospital.

7. It would appear from this study that the mortality and morbidity in accidental or criminal abortion could be reduced materially by more intelligent management of each case from its onset. Such management would include the following of certain principles which experience has shown may not be violated without ill results.

HYPERTHYROIDISM ASSOCIATED WITH MALIGNANT TUMORS OF THE THYROID GLAND

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IN the 249 cases of malignant tumors of the thyroid gland which have been seen at the Cleveland Clinic, the first impression of the examiner in 4 1 per cent of the cases was that a mild or a questionable hyperthyroidism was present. A closer study, however, shows that in only 2 instances was there any indication of hyperthyroidism as based on such objective criteria as persistent tachycardia or elevation of the basal metabolic rate in the presence of a history and physical findings consistent with hyperthyroidism It is not unlikely that the apparent hyperthyroidism in these 2 cases and in similar cases that have been reported by others was the result of one of two factors (a) changes incident to an increase of the patient's vascular bed, or (b) simulation of hyperthyroidism by some systemic disturbance incident to the presence of a large malignant tumor or its metastases

The first of these mechanisms, i e , the simulation of hyperthyroidism by an increase of the vascular bed, is illustrated by the following case in which a malignant adenoma of the thyroid had resulted in a huge, pulsating metastasis to the ilium Although a forceful tachycardia, an elevated basal metabolic rate, and a history consistent with that found in cases of hyperthyroidism were all present, in all probability the patient did not have hyperthyroidism, for the entire picture could be explained on the basis of increased circulation through the large vascular bed of the metastatic tumor

CASE REPORT

The patient was a woman 65 years of age who came to the Clinic on November 6, 1934, because of a tumor of the left hip Since childhood, a large goiter which involved the right side and isthmus of the thyroid gland had been present, but its size had not increased for many years Two and a half years before this examination, the patient began to notice pain in the left hip Six months later, a tumor of the hip was observed, and at about the same time, the patient noticed an enlargement of the left side of her neck.

Preceding this examination, palpitation and tachycardia had been noticed The patient had been more nervous than usual, had lost strength, and, despite a good appetite, she had lost 10 pounds in weight. There had been moderate hyperhidrosis, but no tremor, dyspnea, dysphagia, cough, or hoarseness Recently, the tumor of the hip had given considerable pain, and it was for this reason that the patient sought aid

Physical findings Physical examination revealed a well developed and nourished woman (Fig 1) whose appearance and behavior did not suggest the presence of hyperthyroidism The pulse rate was 120, the blood pressure was 140 systolic and 75 diastolic, and the temperature was 99.4 degrees F The skin was somewhat pale, the hands were warm and dry, and there was no digital tremor No exophthalmos, lid lag, or widening of the palpebral fissures was present Examination revealed a large, soft colloid adenoma of the right lobe of the thyroid gland and a smaller equally soft adenoma of the isthmus Involving the left lobe, there was an extremely hard, fixed, nontender mass 7 centimeters in diameter which presented the clinical features of a malignant tumor The heart was slightly enlarged to percussion, and there was a forceful thrust at the apex A blowing systolic murmur was audible over the entire precordium, but the heart sounds were regular and of good quality The peripheral vessels were moderately thickened The lungs were clear and resonant throughout. On the left hip, fixed to the ilium, there was a huge, expansibly pulsating, firm, non-tender mass the size of a football A thrill and brut were present over the entire mass, overlying veins were dilated Pressure on mass did not slow the heart rate Patient walked with a distinct limp Further significant findings not revealed

Laboratory findings The red blood cells numbered 4,130,000, the hemoglobin was 78 per cent, and the white blood cells numbered 8,500 with 62 per cent polymorphonuclear neutrophils, 1 per cent eosinophils, 23 per cent lymphocytes, and 14 per cent monocytes

Urinalysis showed no sugar or albumin to be present, and only an occasional white blood cell was found. The fasting blood sugar was 104 milligrams, blood urea, 48 milligrams, and the carbon dioxide content was 54.8 milligrams per 100 cubic centimeters On two separate occasions, the blood cholesterol was 185 and 182 milligrams per 100 cubic centimeters, and the blood iodine was 6 16 and 7.46 micrograms per 100 cubic centimeters The Wassermann and Kahn tests gave negative findings

A roentgenogram of the chest revealed the heart to be enlarged There were several small nodules in both lungs which were interpreted as metastatic tumors, probably of thyroid origin A roentgenogram of the pelvis (Fig 2) showed a large, soft tissue tumor mass rising from the ilium Destruction of the bone was so extensive that only a strip 1½ inches wide remained adjacent to the sacro-iliac joint There was also an area of destruction of the ascending ramus of the left tuber ischii

An electrocardiogram showed sinus tachycardia with normal rhythm, an inverted T wave in lead III, and left axis deviation No evidence of myocardial damage.

The basal metabolic rates on three different days were plus 56 per cent, plus 29 per cent, and plus 26 per cent.

At the time of admission to the hospital, the patient's pulse rate was 130, and during the 7 days of observation, although the temperature was never above 99 5 degrees F , the pulse rate ranged from 100 to 110 The diagnosis at the time of discharge was malignant adenoma of the thyroid gland with metastases to the ilium, ischium, and lungs

In this interesting case, many of the clinical features of hyperthyroidism were exhibited The

persistent, forceful tachycardia, the palpitation, the increased pulse pressure, the loss of weight, the good appetite, the loss of strength, the nervousness, the basal metabolic rates of from plus 26 per cent to plus 56 per cent, and the recent enlargement of the pre-existing goiter all seemed to indicate that the neoplastic enlargement of the left lobe of the thyroid gland or its metastases were functioning as thyroid tissue and were inducing an active hyperthyroidism. The tachycardia could not be explained on the basis of respiratory obstruction, anemia, fever or organic heart disease. Yet the blood iodine and the blood cholesterol on two separate occasions were well within the limits of normal—findings which must be interpreted as evidence against the presence of hyperthyroidism.

Since it could not be proved that the tachycardia and the increased basal metabolism in this case were secondary to hyperthyroidism, it is highly probable that they were the result of the increased action of the heart incident to the maintenance of the circulation of blood through the huge and excessively vascular pulsating metastatic tumor of the ilium. It was assumed that the tremendous vascular bed of this tumor with its dilated vessels, pulsation, thrill and bruit had imposed so great a burden upon the heart that this organ was forced to increase its activity thus resulting in a persistent tachycardia and in a mild cardiac hypertrophy. On this basis, the presence of the left axis deviation might also be interpreted as indicating that the left ventricle was doing an excessive amount of work. For the same reason, the total work of the heart was increased, and this increase resulted in increased oxygen consumption by the myocardium, and hence in an increase of the total oxygen consumption of the body and in a proportionate elevation of the basal metabolic rate. All clinical and laboratory findings in this case could thus be correlated on the basis of the increased work of the heart incident to the maintenance of circulation through so large a vascular bed.

Similar studies were made in the case of a woman 53 years of age who had a hypernephroma of the left kidney. The tumor was about 7 inches in diameter and presented an expansile pulsation as well as a palpable thrill and a loud bruit. There was a pulsating metastasis 2½ centimeters in diameter in the clavicle but X ray pictures of the skull, chest, and spine revealed no further metastases. The pulse was consistently over 100 when the patient was at rest in bed, the blood pressure was 160 systolic, 70 diastolic, and duplicate basal metabolic rate determinations averaged plus 28 per cent. The blood iodine and cholesterol were within normal limits, and the appearance of the patient did not suggest the presence of hyperthyroidism. Since there was no fever and no abnormality of the blood, heart, or lungs to account for the persistent tachycardia, the increase of pulse pressure and the elevation of the basal metabolic rate, it was concluded that here again the increase of the vascular bed caused elevation of the basal metabolic rate.

In order to test this hypothesis, studies were made of a man 26 years of age who, for the past 10 years, had had a gradually enlarging arteriovenous aneurism of the carotid artery. The lesion was of traumatic origin and there was no associated disease or complication. This patient had a forceful tachycardia similar to that seen in the case just mentioned: the pulse rate ran as high as 130 and stayed consistently above 100 when he was at rest in bed. The blood pressure was 130 systolic and 65 diastolic. The basal metabolic rate on two occasions was plus 30 per cent, but the blood iodine was within normal limits (9.5 micrograms per 100 cubic centimeters) and there was no clinical evidence of hyperthyroidism. It is apparent that here the excessive work imposed upon the heart by an arteriovenous fistula, just as in the first case the excessive work incident to supplying a large dilated vascular bed, had resulted in a persistent tachycardia and in an elevation of the basal metabolic rate.

REVIEW OF LITERATURE

There is no agreement in the literature regarding the incidence of the association of hyperthyroidism with malignant tumors of the thyroid gland. Bérard and Dunet state that all the classical symptoms of hyperthyroidism are almost never seen in association with cancer of the thyroid gland, but they add that tachycardia alone is not infrequently observed and that tremor sometimes occurs. These authors state that exophthalmos associated with a malignant thyroid tumor has only very rarely been reported and that they have not seen a single instance of such a case. In the American literature, a higher incidence of the association of hyperthyroidism with malignant tumors of the thyroid gland is reported. Simpson states that one-half his cases of malignancy of the thyroid gland have been associated with hyperthyroidism, and that he has seen 5 cases in which exophthalmos was present. Simpson concludes that in his cases, the "symptoms of hyperthyroidism have been produced by the secretion from the actively proliferating thyroid carcinoma cells."

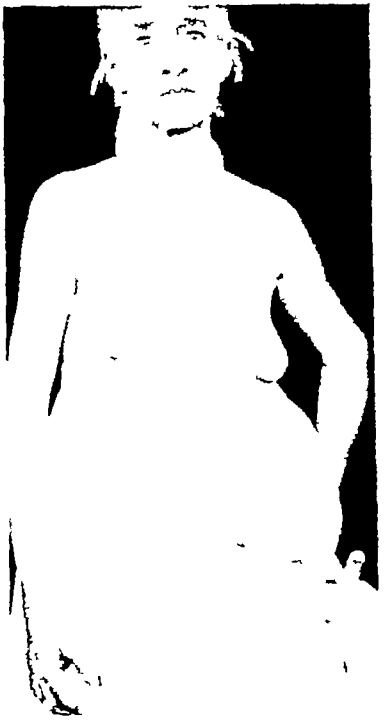

Fig 1 Photograph of patient

Fig 2 Roentgenogram of pelvis showing large tumor and destruction of ilium

Coller states that the commonest complaints in his series of cases of malignancy of the thyroid gland were of those symptoms which usually are associated with hyperthyroidism, such as nervousness, loss of weight, tachycardia and palpitation—symptoms which were present in 47 per cent of the cases In 44 per cent of the cases, the basal metabolic rates ranged from plus 16 per cent to plus 80 per cent Coller concludes, ' The fact that most of these patients had basal metabolic rates that were normal or above normal suggests that malignant thyroid tissue may retain some of its original function "

Boothby found definite evidence of hyperthyroidism by a study of the basal metabolic rates in 22 per cent of 45 known cases of malignancy of the thyroid gland seen at the Mayo Clinic Herbst, however, from the same clinic, could find clinical evidence of hyperthyroidism in only 3 per cent of the cases, and he states that there was no case of carcinoma of the thyroid gland in 5,867 cases of exophthalmic goiter

Eberts (4, 5) has reported 2 cases in which active hyperthyroidism was associated with a malignant tumor of the thyroid gland, but he admits that the histology of these tumors was not typical of thyroid malignancy and states that since both patients were alive and well, 3 and 4 years, respectively, after operation, even more doubt is thrown upon the true nature of the tumor

Pemberton concludes that the basal metabolic rate is influenced more by benign than by malignant tumors of the thyroid gland He explains the occasional association of hyperthyroidism and malignant tumors by the fact that 87 per cent of the malignant tumors of the thyroid gland arise in adenoma which may or may not be associated with hyperthyroidism This idea is in harmony with the findings of Marine and Johnson and of Eisen, who showed that in a series of cases of malignant tumors of the thyroid gland, metastasizing tumors did not exhibit the normal thyroid function of taking up and storing iodine

Graham, in discussing tumors of the thyroid gland, has stated "It is the transformation of adenoma to carcinoma that constitutes the entity The innumerable morphological variations possible in a series of tumors or even in a single tumor are but circumstances in the process " This interpretation of thyroid neoplasms would explain the occasional association of hyperthyroidism with a malignant tumor of the thyroid gland as representing the development of the malignant tumor in a previously "toxic" adenoma However, there still remains the problem of reconciling the diverse opinions regarding the incidence of hyperthyroidism in malignant tumors of

the thyroid gland. Some writers place this incidence as low as 3 per cent and others as high as 50 per cent. It is my belief that misinterpretation of symptoms suggestive of hyperthyroidism, or differences in the pathological interpretation of tissues removed at operation are responsible for this divergence of opinion. Since a study of the pathological changes of the thyroid gland does not fall within the scope of this paper, I shall merely point out some mechanisms by which a malignant tumor of the thyroid gland can produce a clinical picture which closely simulates that of hyperthyroidism.

DISCUSSION

The type of tumor which attains sufficient size and vascularity to be able to produce systemic effects by overtaxing the circulatory mechanism as in the cases reported here must be relatively rare. It is nevertheless quite probable that a number of patients, in whom large vascular malignant thyroid tumors and a secondary tachycardia were present, have been thought to have been suffering from hyperthyroidism and have been reported in the literature as cases of hyperthyroidism associated with malignant thyroid tumors.

The other type of case in which the presence of a malignant tumor is apt to result in a clinical picture that can be confused with hyperthyroidism is seen when there are systemic manifestations of extensive malignant disease. Pertinent data can be found in examining case records of malignant tumors of organs other than the thyroid gland. The history of loss of weight, nervousness, tremor, fatigue and palpitation is unusual in the presence of any advanced malignancy. Since the presence of an advanced malignant tumor of any organ can result in a syndrome which suggests the presence of hyperthyroidism, it is not surprising that when the tumor involves the thyroid gland hyperthyroidism is even more strongly suggested and the clinical picture is interpreted as the expression of a mild hyperthyroidism.

As has been stated there are only two instances in a series of 249 cases of malignant tumors of the thyroid gland in which examination of the record shows any objective evidence of an associated hyperthyroidism. In the first of these 2 cases, the tumor was a large rapidly growing degenerating carcinoma so undifferentiated that it was at first considered to be a sarcoma. In this case there is almost no possibility that the undifferentiated tumor tissue could have been able to function. It is probable therefore that the symptom represented the systemic effects of extensive malignant disease or were the result of a coincidental overactivity of the uninvolved portion of the thyroid gland. Since the symptoms were very mild, since in spite of a single basal metabolic rate of plus 25 per cent the clinical features of hyperthyroidism were not present, and since the remaining portion of the thyroid gland was in a pure colloid phase the probabilities are that the clinical findings in this case were secondary to absorption from the large degenerating tumor or its metastases.

The second case in which hyperthyroidism appeared to be associated with a malignant tumor of the thyroid is an example of a malignant tumor developing in an adenoma which for several years had shown questionable signs of mild activity. The patient was a man, 56 years of age who first had noticed nervousness and irritability in 1915, 2½ years before our examination. Enlargement of the neck was not observed until 2 years after the onset of these symptoms. In the 6 weeks prior to entry he had lost 30 pounds in weight and tachycardia, dyspnea on exertion and tremor had developed.

Physical examination revealed the presence of a hard, nodular goiter of moderate size, tachycardia, and a slight, fine digital tremor. A diagnosis of nodular goiter with moderate hyperthyroidism was made and ligations of both superior thyroid arteries were performed.

The patient returned 3 months later symptomatically unimproved. Subtotal thyroidectomy was performed and the pathological diagnosis of the specimen removed was malignant adenoma of the thyroid. The tumor was well differentiated and in addition it arose in an adenoma, certain areas of which were definitely hyperplastic.

Following thyroidectomy the patient made striking improvement and gained 38 pounds. Three months after the operation in spite of the fact that no mention of recurrence of the patient's hyperthyroidism was made the pulse rate was still constantly above 100 when the patient was at rest in bed. Bone metastases were discovered 2 months later and the patient died with bone and pulmonary metastases 2 years after the thyroidectomy had been performed.

The evidence on which we based the diagnosis of hyperthyroidism in this case is not strong yet the case is included because it presents the most clear-cut picture of hyperthyroidism that is to be found in the records of the 249 malignant tumors of the thyroid gland in this series of cases. In this case there is no record of the basal metabolic rate of the blood cholesterol, or of a blood iodine determination. Tachycardia was nearly as pro

nounced after the operation as before, and soon after thyroidectomy, evidences of generalized metastases were seen

As we have pointed out, great care must be exercised in making a diagnosis of hyperthyroidism in the presence of generalized metastases It is, therefore, not improbable that this patient's symptoms were largely the direct result of the malignant disease rather than of a true hyperthyroidism induced by functional activity of the thyroid tumor and its metastases

The basal metabolic rates in a recent series of 33 cases of malignant adenomas and of papillary carcinomas of the thyroid gland averaged plus 0 3 per cent These two types of neoplasm are the most highly differentiated forms of thyroid malignancy and hence probably represent the type of tumor most likely to show functional activity Yet in only 3 cases was the basal metabolic rate above plus 16 per cent One of these 3 patients had an elevation of temperature associated with extensive pulmonary metastases The second patient suffered from dyspnea secondary to tracheal compression, the third was the case herein reported in which a large pulsating metastatic tumor was present in the ilium In no case was there clinical evidence of hyperthyroidism In 4 cases, the basal metabolic rate was below minus 16 per cent It has been found, therefore, that in this series of malignant tumors of the thyroid gland, there was no consistent deviation from the normal basal metabolic rate

In conclusion, it can be said that in 249 cases of malignant tumors of the thyroid gland, there was not a single instance of the indisputable coexistence of hyperthyroidism The rareness of the association of these two conditions suggests that this association is largely coincidental, the two diseases probably bearing no etiological relationship to each other It must follow, therefore, that the diagnosis of hyperthyroidism should be made with caution in the presence of a thyroid gland which has the characteristics of a malignant tumor, and that, conversely, the diagnosis of malignancy should be made with equal hesitancy in cases in which there is unequivocal evidence of active hyperthyroidism

SUMMARY

1 There is a lack of agreement in the literature regarding the incidence of hyperthyroidism associated with malignant tumors of the thyroid gland

2 This disagreement can probably be explained (1) by differences in opinion among pathologists as to the criteria of thyroid malignancy, (2) the tendency, in the presence of goiter, to attribute to hyperthyroidism the symptoms and signs which are in reality the result of extensive malignant disease

3 The mechanism whereby a large vascular tumor can produce a tachycardia, an increased basal metabolic rate, and a syndrome suggestive of hyperthyroidism is discussed, and a case is reported in which these findings were present

4 There is no case in a series of 249 malignant tumors of the thyroid gland which shows a picture of unequivocal hyperthyroidism that cannot be explained as being the result of either (a) increased circulation through a large vascular tumor, or (b) systemic effects of extensive malignant disease

5 The average basal metabolic rate of 33 patients with malignant tumors of the thyroid gland was plus 0 3 per cent

6 The diagnosis of malignant tumor of the thyroid gland should be made with hesitancy in cases in which there is evidence of active hyperthyroidism

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SKELETAL TRACTION AND COUNTERTRACTION METHODS

Used in Ordinary Extension Splints in Treatment of Fractures of the Long Bones[1]

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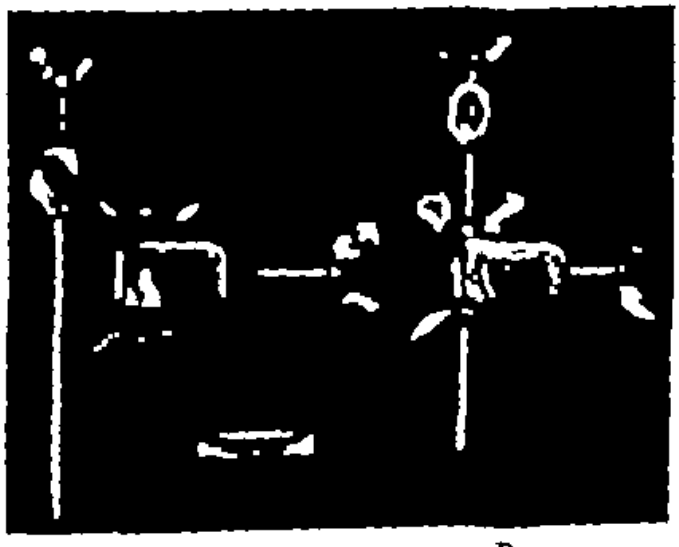
ALL of the present devices combining skeletal traction and countertraction are dependent upon a supporting frame, a part of the apparatus itself, to support the fractured extremity during the period of active traction and countertraction. Although these methods of treatment are excellent from a mechanical standpoint, there is one objectionable feature, the cost of the apparatus, which is due largely to the necessary supporting frame. The cost of the apparatus, therefore, is an obstacle to its general use by the average surgeon or hospital.

Because of the relatively high cost of the apparatus now in use, I have devised a more simple and economical means of applying skeletal traction combined with skeletal countertraction to *ordinary extension splints. The simple and inexpensive* device herein described makes this possible by utilizing only those extension splints commonly used in the average hospital. For this purpose one may use either a Thomas or Hodgen splint and the Bohler Braun frame (2) for fractures of the tibia and fibula and for fractures of the femur and the Clayton extension splint for fractures of the bones of the forearm.

My apparatus consists of two pairs of adjustable clamps, each clamp or unit being of similar pattern. Each pair of clamps serves to hold a transfixion pin or rigid wire in tautness to the supporting splint or frame. The pair of clamps holding the countertraction pin or wire in tautness are firmly secured to the rods of the splint or frame. The pair of clamps holding the distal or traction pin or wire in tautness are fixed to a sleeve placed over the side rods of the splint or frame. These sleeves to which the clamps are applied allow free play of the distal pin or wire in tautness while undergoing traction.

The apparatus is used with continuous traction by means of weight and pulley. It is the only device known to the writer to retain the principles of Buck's continuous extension with the exception of the spring traction in the apparatus of Hawley (4). This point is important because I am convinced that continuous traction by either weight and pulley or spring traction is superior to the so called intermittent or screw traction. This is particularly true of old fractures with shortening in which restoration of the length of the extremity can be obtained only by means of gradual and prolonged continuous traction.

The shifting proximally or distally of the clamps holding the countertraction pin or wire, together with the raising or lowering of opposite ends of



A B

Fig. Photograph showing pin or tautner holding clamp with split sleeves. A, unassembled; and B, assembled.

Fig. 1. Showing set up with slightly modified Hodgen splint placed on an ordinary but cut out orden box. This arrangement may be used instead of suspended Thomas or Hodgen splint, a Bohler Braun frame, or the new and more expensive apparatus used in combining skeletal traction and countertraction.

From the Surgical Service, U. S. Marine Hospital, San Francisco, California.

Fig 3 Case 1 Fracture of both bones of leg, treatment instituted about 24 hours after injury Bohler pins inserted through upper end of tibia and the calcaneum and leg suspended in Thomas splint by means of the pin holding clamps Continuous traction by means of weight and pulley A non padded plaster cast, incorporating transfixion pins applied 3 days later See Figure 8 showing satisfactory reduction

Fig 4 Case 2 Fracture of femur followed by malunion (3½ inches shortening and 40 degrees' angulation) Injury about 7 months before admission to hospital Patient also had had an amputation below the knee on account of a compound fracture of both bones of the leg The photograph shows the extremity suspended in a Thomas splint with an extra large ring piece and padding removed The Bohler pins are seen inserted through the femur just below the trochanters and just above the epicondyles Preliminary osteotomy separated the distal fragment from the third fragment firmly united to the upper fragment Continuous skeletal traction of 30 pounds by weight and pulley with skeletal countertraction maintained for 12 days gradually restored full length to the femur (see Fig 9 B) Then by open operation, interposing soft tissue was removed, reposition of the fragments was secured, and the third fragment, after osteotomy and only partial detachment from surrounding soft parts, was forced down alongside the ends of the major fragments with the idea of this third fragment serving as a bridge over the fracture site

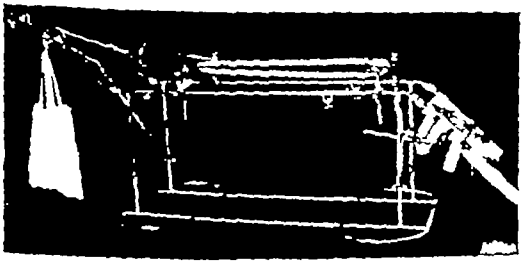


Fig 5 Photograph showing Zimmer modification of Bohler Braun frame to which have been attached pin or tautner holding clamps for skeletal traction and counter traction—continuous traction by means of weight and pulley

the traction and countertraction pins or wires greatly facilitates reposition and alinement of the fragments, an accomplishment similar to the Roger Anderson (1) and Griswold (3) splints After satisfactory reduction of the fracture has been obtained, the clamps holding the distal or traction pin may be locked to the rods of the splint or frame, and the weights and pulleys

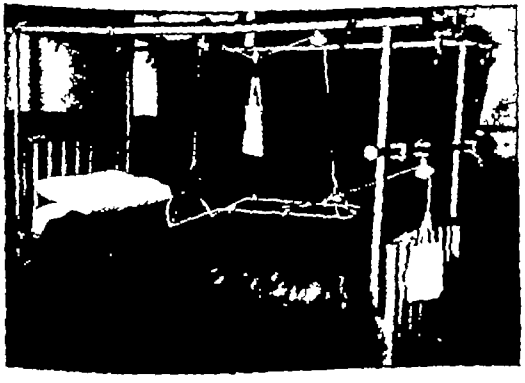


Fig 6 Showing adjustable clamps attached to Hodgen splint suspended to overhead frame This set up is ideal for fractures of both bones of the leg as the splint provides for flexion of the knee

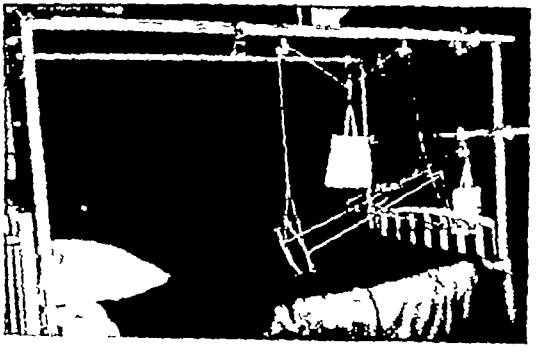


Fig 7 Showing adjustable clamps attached to Thomas splint with an enlarged ring piece with padding removed and with Pearson leg attachment, suspended from overhead frame. This set up is ideal for fractures of femur with marked shortening

Fig 8 Case 1 Roentgenogram of fracture of both bones of leg, before left, and after treatment, right, with my device, showing perfect reposition of fragments

Fig 10 Case 3 Roentgenogram of fracture of both bones of leg, before, left, and after treatment, right, with my device showing perfect reposition of fragments. (Courtesy of San Francisco Hospital)

A B C

Fig 9 Case Roentgenogram of fracture of femur followed by malunion A, before preliminary osteotomy of distal fragment B, 12 days later restoration of full length by means of 30 pounds continuous skeletal traction combined with skeletal counter traction C, after open operation to remove interposing soft tissue and osteotomy of third fragment, continuous traction of 8 pounds by weight and pulley used to maintain the reposition and to immobilize the fragments

removed A non-padded plaster cast then may be applied to the extremity incorporating the transfixion pins or wires In compound fractures, the extremity may be left suspended for a longer period before encasement in plaster

When my device is used with the Thomas extension splint the skeletal countertraction eliminates the pressure of the ring piece against the ischial tuberosity and also prevents an ill-fitting ring piece from pressing against the perineum. This greatly facilitates the use of the bed pan, simplifies the sanitary care, and adds greatly to the comfort of the patient

The illustrations, Figures 1 3 4, 5 6 and 7 showing the clamp unassembled and assembled, and as used with the Thomas and Hodgen splints and the Bohler Braun frame are self explanatory

Roentgenograms with explanatory notes in three cases in which my device has been used are shown in Figures 8 9 and 10.

SUMMARY

1 A description is given of a simplified and inexpensive apparatus to use with ordinary hospital extension splints for combining skeletal traction with skeletal countertraction for fractures of the long bones.

2 The apparatus is used with continuous traction by means of weight and pulley and is the only device known to the writer to retain the princi-

ples of Buck's continuous extension with the exception of the 'spring' traction in the apparatus of Hawley

3 The apparatus is believed to furnish the best means of overcoming, after osteotomy, the shortening found in old malunited fractures of the long bones

4 The apparatus when used with the Thomas extension splint, eliminates the pressure of the ring piece against the ischial tuberosity, thereby simplifying the sanitary care and adding to the comfort of the patient

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A METHOD FOR RE-EXPANSION OF THE COLLAPSED LUNG IN EARLY OR LATE EMPYEMA

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THE purpose of this report is to describe a simple, inexpensive method for passively re-expanding the collapsed lung in cases of early chronic empyema when no bronchial fistulas are present.

It is obvious, from a consideration of the physiology of respiration, that the degree of expansion of the lung is dependent on the balance of intrapulmonary and intrapleural pressures mechanical factors such as elasticity of the lung tissues, pleural thickening and adhesions between the visceral and parietal pleura being considered as constant This concept is utilized in the production of a partial or complete collapse of the lung in the induction of artificial pneumothorax in which instance the intrapleural pressure is increased The reverse situation obtains in the respiratory exercises, such as forced expiration against pressure, used in the treatment of pleural empyema, in which case the intrapulmonary pressure is increased in an attempt to re-expand the collapsed lung This, however, is an active procedure and has as the upper limit of a maintained increased intrapulmonary pressure the capacity of the respiratory muscles for work

During normal inspiration the volume of the thoracic cage is increased so that the interpleural pressure becomes less than the intrapulmonic pressure and air rushes into the bronchi and expands the lungs This process may be mechanically duplicated by the application of suction in the interpleural space so that the lung may be maintained in a state of continuous distention by the maintenance of a decreased interpleural pressure

In cases of chronic empyema, the lung remains collapsed as a result of the presence of a complete pneumothorax (when the interpleural and intrapulmonic pressures are equal), and this collapsed state of the lung is also maintained by the presence of a thickened inelastic visceral pleura and possibly by changes in the elastic characteristics of the collapsed lung substance If a pleural exudate is present, this will act further to compress the lung substance

If, however, the interpleural pressure can be sufficiently reduced by continuous suction, the effect of the pneumothorax is overcome and the fibrous, thickened visceral pleura may be stretched so that the collapsed lung can be re-expanded

METHOD

The source of suction is readily obtained by a modification of the Wangensteen suction apparatus (Fig 3) A rubber suction cup attached as shown in the diagram is placed against the chest wall to cover completely the opening in the chest wall The edges of the cup are ringed with petrolatum jelly The clamps *A* and *B* are then opened, and the degree of suction applied is represented by the distance in centimeters of water between the water levels of the upper and lower bottles The soft tissues of the chest wall are drawn outward into the cup, and the cup is maintained firmly in place by the difference between atmospheric pressure and the reduced interpleural pressure After suction has established a constant level of interpleural pressure, clamps *A* and *B* may be closed and the suction cup may be separated from the suction apparatus

Fig. Chest roentgenograms taken before and during the application of siphon suction at the left pleural space on May 17, 1935. The collapsed left lung and complete left sided pneumothorax with the drainage tube in place can be seen in the chest film before suction. After the application of siphon suction, shift of the left lung border outward and resultant decrease in size of left pleural empyema cavity as well as shift of the trachea to left, can be seen.

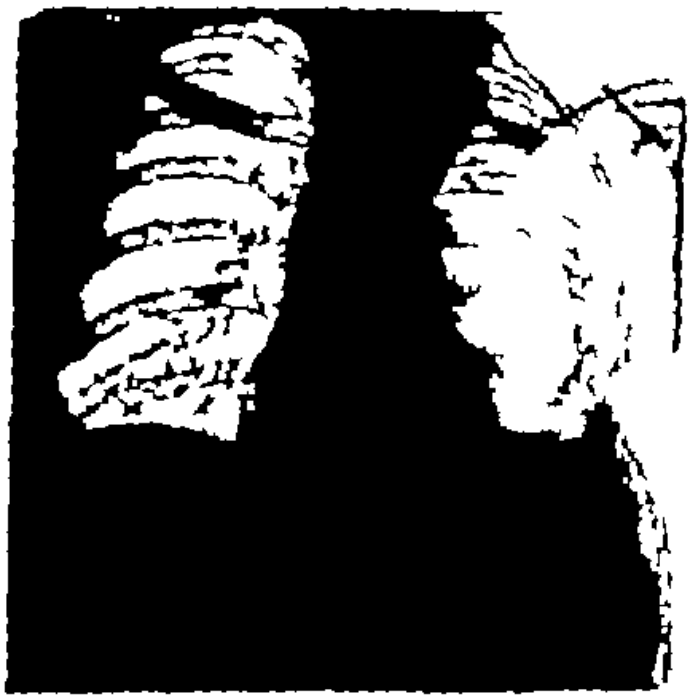

Fig. 2. Chest film taken on July 2, 1935, showing complete re-expansion of the left lung and moderate thickening of the pleura.

at the rubber and glass tube junction. The decreased interpleural pressure may be maintained for several hours daily while the patient lies quietly in bed. If leakage of air should occur about the margin of the rubber suction cup, the subatmospheric interpleural pressure is increased to the atmospheric pressure level and the rubber cup falls off the chest wall.

The suction at first is started with the difference in water levels of the upper and lower bottles at 30 centimeters. With this degree of suction the patient may complain of a deep drawing sensation under the sternum which is very probably due to traction on the mediastinum causing displacement *toward the side of suction. The lower* bottle may gradually be lowered from day to day and the pressure in the interpleural space be made gradually more subatmospheric so that a difference in tension of 2 meters of water between interpleural and intrapulmonary pressures may readily be tolerated within 10 days to 2 weeks.

Between the periods of the application of suction to the interpleural space the lung partially collapses but the potential expansibility of the lung is gradually increased by stretching the thickened visceral pleura. *The empyema* cavity

becomes progressively smaller and is finally obliterated by the formation of adhesions between the thickened visceral and parietal pleura

The contra-indications and possible dangers of the siphon suction treatment of early or late chronic empyema are

1 The presence of a bronchial fistula, in which instance air rushes from the intrapulmonary to the intrapleural space, and suction cannot be maintained

2 The possibility of hemorrhage resulting from sudden and excessive degrees of decreased interpleural pressure. To avoid any possibility of tearing small vessels or even the lung substance itself, the difference between interpleural and intrapulmonary pressures should be slight at first and gradually increased

3 The possibility of a sudden marked mediastinal shift with torsion of the vessels at the base of the heart which may lead to circulatory disturbances The mediastinum is, however, more rigid than normal in these cases and the possibility of a rapid shift is remote

The method which has been described seemed worthy of trial since it had been determined on this service that the use of the suction side of the Drinker respiratory apparatus had been beneficial in re-expanding the collapsed or retracted lung The method of continuous siphon suction for the treatment of chronic empyema has been used in a single case with results which appear worthy of a report.

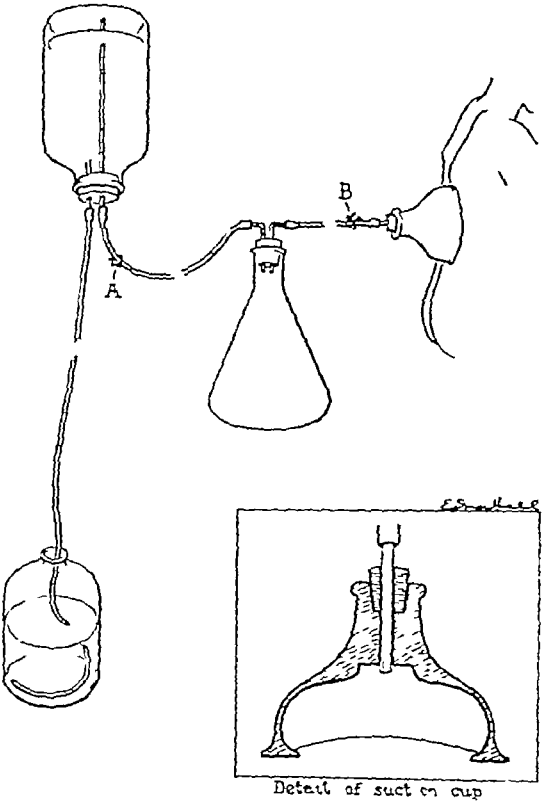

Fig 3 Diagram of siphon suction apparatus and cross section of suction cup The upper bottle is suspended from a stand and the lower bottle is placed on a table The suction cup consists of a moderately firm rubber cup (sold in hardware stores to clean out clogged drain pipes) approximately 5 inches in diameter A rubber cork is fitted into the cup and a hole is drilled through the cork and cup and a glass tube is introduced into the cup as shown in the cross section This glass tube is connected by firm rubber tubing to the suction apparatus

The patient, a white female 29 years old, viii para in the third month of pregnancy, was admitted to the medical ward of the Hospital of the University of Pennsylvania, March 10, 1935 Two days before admission the patient had left pleural pain, dyspnea, and fever Physical examination revealed signs typical of frank consolidation of the left lower lobe Examination of the sputum revealed pneumococci subsequently identified as group IV A diagnosis of left lower lobe pneumococcus pneumonia was made and confirmed by roentgen ray examination Artificial pneumothorax was induced and two refills were done within 36 hours with an initial drop in temperature and clinical evidence of improvement The chest film after pneumothorax showed collapse of the left upper lobe and considerable mediastinal shift. Four days later there was a resumption of a febrile course and a chest film confirmed the clinical impression of the presence of a left pleural effusion. Repeated thoracentesis during the course of the next 2 weeks yielded purulent fluid which gradually increased in viscosity, and the patient was transferred to Surgical Service "E," April 6 1935 Internal drainage was instituted in the seventh interspace in the posterior axillary line on the left side and the Overholt modification of the Deryl Hart apparatus was used for drainage The purulent fluid became more viscid and on April 23 1935, rib resection was performed and two drainage tubes were inserted The empyema cavity was irrigated with Dakin's solution, and postural exercises and expiration against pressure by the use of blow bottles were used in an attempt to re-expand the collapsed left lung A chest film on April 30, 1935 revealed complete collapse of the left lung and some thickening of the pleura In spite of the conventional exercises, there was little apparent change in the appearance of the chest on May 15, 1935, when continuous siphon suction was applied

When suction was applied, the breath sounds were markedly increased in amplitude, and numerous râles were heard over the left lower lobe. These changes disappeared when suction was discontinued The left lung was observed under the fluoroscope, and a definite degree of expansion occurred after the application of suction to the interpleural space Chest films were taken before and during the application of suction (Fig 1), and a definite shift of the left lung border outward away from the cardiac silhouette was observed The superior mediastinum was shifted slightly to the left With the continued intermittent application of siphon suction the left lung gradually re-expanded and almost completely filled the left thoracic cage at the time of discharge June 17, 1935 Three weeks

after siphon suction was started the wound was entirely closed and no drainage was present

The patient was again examined on July 12, 1934, and roentgen-ray examination revealed complete obliteration of the left pleural space and moderate thickening of the pleura (Fig 3) The site of the thoracotomy was completely healed and clinically the patient was well

SUMMARY

1 A method for the application of siphon suction to the interpleural space to re-expand the collapsed lung in cases of early and late chronic empyema thoracis has been described.

2 The results of siphon suction therapy in a case of early chronic pleural empyema have been presented.

3 It is suggested that the method of siphon suction be used in cases of early or late empyema to re-expand the collapsed lung

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AN ASEPTIC METHOD OF TEMPORARY VALVULAR ENTEROSTOMY[1]

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THE practice of performing valvular enterostomies has largely obviated the possibility of persistent fistulous formation. The desideratum, then is a method whereby these intestinal stomas may be produced without exposing the peritoneum and abdominal wall to potential contamination by the intraluminary contents This possibility although rarely productive of lethal consequences, is nevertheless an ever present hazard and a decided factor in morbidity Recent reports of the incidence and fatalities from gas bacillus infection complicating enterostomies are concrete illustrations (12)

Decompression of the intestine was deliberately done for relief of disease as early as the 16th century, when Ambroise Paré pricked the distended bowel with a needle for the purpose of assisting in the reduction of strangulated hernias (11) The success of this procedure, according to Saunders, probably suggested puncture of the intestine through the intact abdominal wall for relief of tympanites from any cause (11) This practice became widespread but seemed to find its greatest value as an euthanasic rather than a therapeutic measure for Morgagni definitely pointed out in 1761 that should agglutination of the visceral and parietal peritoneal surfaces fail to occur intestinal contents might escape into the abdomen and be the direct cause of a fatal result In 1757 Lewis had recommended a more deliberate surgical procedure, but it was not until 30 years later that enterostomy or enterotomy as it was formerly called, was first used by Renault, i.e., in 1787 The operation was revived by Nélaton in 1840, who devised a very ingenious method The first loop of presenting distended intestine was sutured to the abdominal wound by two rows of interrupted sutures It was opened immediately or some hours later as the condition warranted In this way soiling of the peritoneal cavity was prevented Thus it might be said that Nélaton established the technique of enterostomy

However it was the work of Fuhr and Wesener in 1886 of performing enterostomy for relief of ileus, with that of Schede in 1887 of sidetracking the fecal current during extensive operations on the intestine below (14) which marked the beginning of the era of temporary intentional fistulas. But closure of the stomas necessitated a secondary operation, either intraperitoneally or extraperitoneally for re-establishment of intestinal continuity

Many surgeons have described numerous methods and established principles which have been utilized in circumventing this difficulty, among them being Moynihan, Lund, Lord, Lusk Long Horsley and more recently Hendon. However Enselsberg in 1895, was the first surgeon to apply the principles of the Witzel gastrostomy to enterostomy But the procedure which seems to hold greatest favor and proves most uniformly successful is that described by C. H. Mayo in 1917 In this, the intestine is emptied of its gas and fluid content by compression with the hand, rubber covered clamps are applied to prevent gross spillage, and a rubber catheter is inserted and transfixed to the bowel wall. The tube is enfolded after the technique of Witzel, and a strip of omentum is interposed between the bowel and the anterior abdominal wall. Orr and others have

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supplemented this method by aspirating the contents of the distended loop by a fine needle A solid tapered tip catheter has usually been preferred for enterostomy, instead of one with a hollow tip or plain rubber tubing, since insertion is facilitated and the wound in the intestine may be proportionately smaller, and the size originally advocated by Mayo was a No 10 to 12 French However, there is a constriction in the lumen of the standard commercial catheter which was found to retard the flow materially in a majority of a series examined Therefore, the present tendency appears to be toward selection of larger sizes, namely Nos 16, 18, or even No 20, the advantage of the smaller tube being sacrificed in order to secure adequate drainage

The method of temporary enterostomy now proposed requires the use of a length of No 14 rubber catheter drainage tubing, to one end of which is attached a conical metal tip with multiple countersunk openings, and to the other a simple "slip-on" connector (Fig 1) This size tubing was selected since a simple siphonage experiment demonstrated that drainage therefrom was as great as that from a No 18 intact catheter and the addition of the metal tip did not materially decrease the flow This rubber tube ensheaths a metal cannula, which in turn is occupied by a metal obturator with a trocar point (Fig 2), the metal parts being of sufficient size to produce a "working fit" within the tube The proximal end contains a simple coil spring and valve which render the instrument practically air-tight (Fig 3)

An area of bowel wall approximately 1 5 centimeters in diameter is encircled by a pursestring suture, placed opposite the mesenteric border, attempting to catch a bit of the submucosa with each stitch A second pursestring is applied in an opposite direction, immediately surrounding the first, the free ends of both being left long to serve as traction sutures A single circular suture may be used, however, the two closely approximated concentric ones give greater security and ease of execution and do not utilize an undue amount of bowel The tip of the instrument is placed in the center of the circumscribed area and held fairly firmly against the bowel at a 90 degree angle with the long axis of the intestine (Fig 4) The elasticity of the wall permits burying of the conical portion of the tube as traction on the sutures is made The first pursestring is drawn up and tied somewhat snugly around the base of the metal tip The obturator is depressed, thereby puncturing the intestine, and then released, so that the bowel is protected from damage The tube is

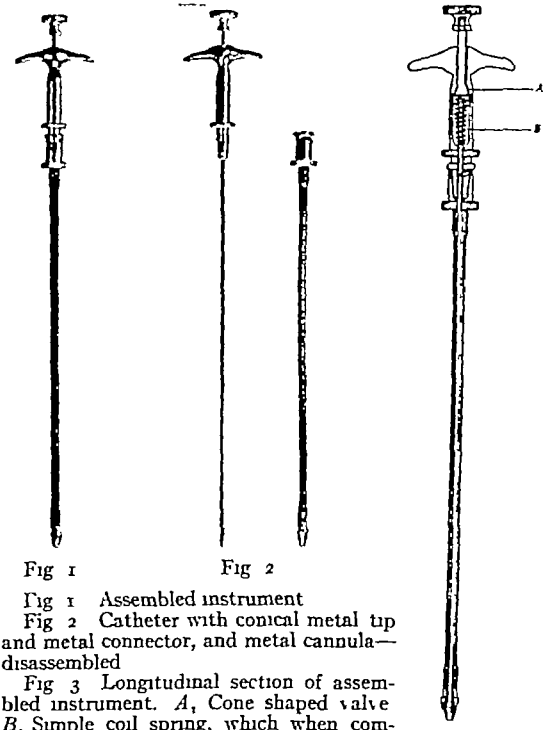

Fig 1 Fig 2 Fig 3

Fig 1 Assembled instrument

Fig 2 Catheter with conical metal tip and metal connector, and metal cannula—disassembled

Fig 3 Longitudinal section of assembled instrument. *A*, Cone shaped valve *B*, Simple coil spring, which when compressed causes the obturator to protrude through the metal tip, and upon being released causes retraction of the cutting point into the cannula

guided with a rotary motion through the opening made by the trocar for a distance of 1 or 2 centimeters (Fig 4, insert) The tautness of the bowel wall, and the right angle direction of the entering instrument will prevent any tendency toward separation of the muscular and submucosal layers of the intestine The angle of the instrument is then changed to about 60 degrees from the norm in the cephalad direction, and it is again guided into the lumen of the bowel for another 1 or 2 centimeters, making a total of 3 or 4 centimeters (Fig 5) The second pursestring is tied, and the ends of both cut short The instrument is then depressed and made to parallel the long axis of the bowel, its rigid metal parts serving as a staff around which the bowel enfolds itself, thus facilitating the insertion of the continuous mattress suture This suture should begin 0 5 centimeter distal to the point of exit of the tube, after the technique of Mayo-Witzel, and continue proximally for about 3 centimeters (Fig 6) With this technique a decided inverted cone is produced, and the valve effect augmented with the tract lined by serosa to its termination (Fig 6

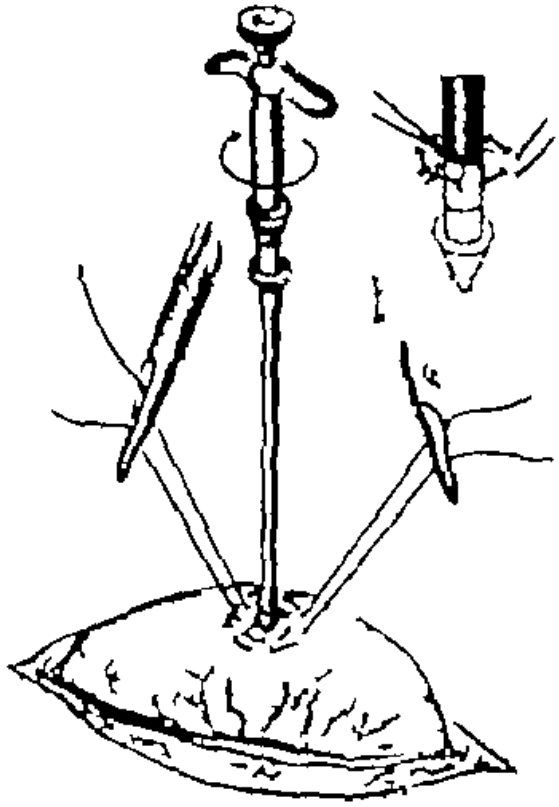

Fig 4 Position of instrument and direction of traction on the sutures which facilitate invagination of the conical tip Insert, Perforation of the intestine has been completed and the instrument guided into the opening

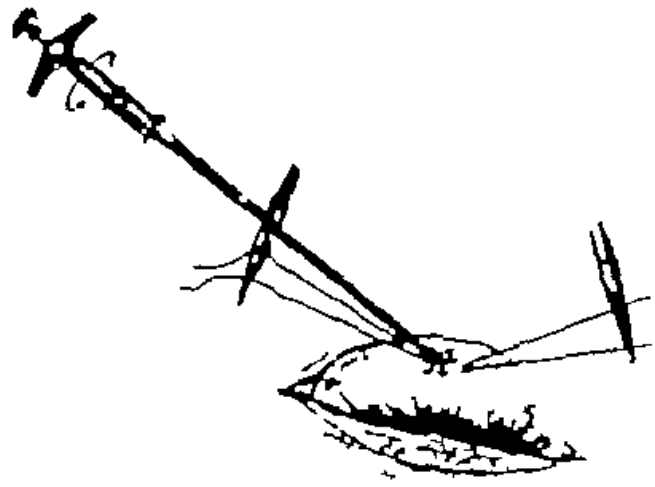

Fig 5 The angle of the instrument changed to about 60 degrees from the norm, and it is being introduced somewhat farther into the lumen by rotary motion

Insert) After the suture is secured, the needle arm is passed through a section of great omentum and parietal peritoneum near the wound edges and again tied as described by Mayo The wound is closed with interrupted sutures—the tube and instrument having been brought out through the dependent portion A long strand of silkworm gut or silk is looped around the tubing at the point from which it emerges from the wound. It is tied with sufficient snugness to seat itself in the rubber the ends being secured to the abdominal wall by adhesive plaster This snubbing stitch may be passed through the skin experience has shown, however that it usually not only "cuts out and delays convalescence, but produces an unsightly scar The metal cannula

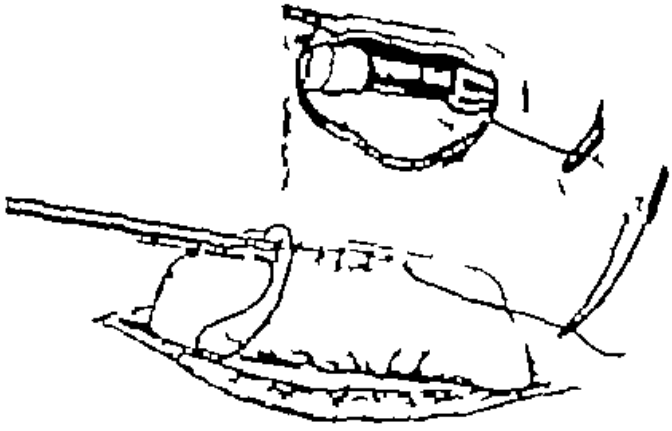

Fig 6 Position of the rigid instrument which renders less difficult the application of the enfolding suture Insert Sectional view of the inverted cone

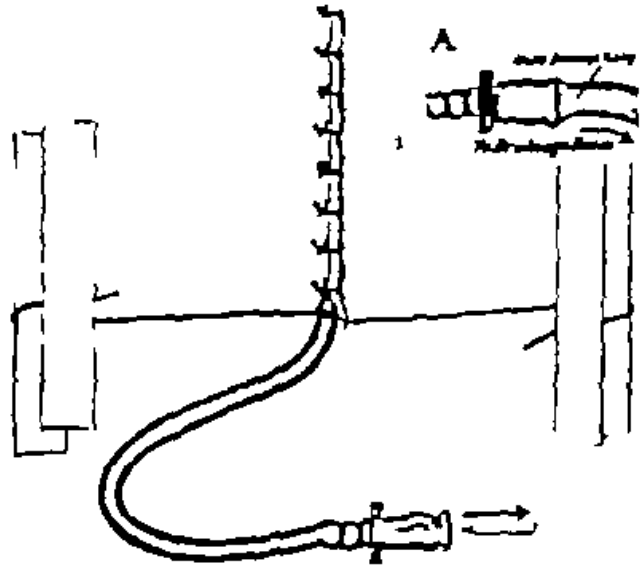

Fig 7 Wound closed, the metal cannula removed from the tube and the insert indicates the manner of connecting additional drainage tubing

is then withdrawn from the tube and drainage established (Fig 7)

It will be noted that in this technical procedure, rubber covered clamps, with the necessary "milking" of the intestine, are dispensed with Sabin has shown that even in normal bowel there is mottling of the cytoplasm of smooth muscle fibers when clamps are applied, no matter how gently This should stress the importance of minimizing traumatism at all times, but particularly whenever the bowel has become attenuated, poorly nourished and its permeability greatly increased from overdistension For this reason, in those instances in which the intestine is so adherent as to preclude easy delivery of the segment from the peritoneal cavity, this method is particularly indicated There is no necessity for anchoring the tube by transfixing it to the bowel, since the oblique position of the tube in relation to the long axis of the bowel is such as to overcome internal pressure, and the silkworm gut anchoring suture is protection against moderate external force Further, by avoiding the transfixing suture, capillary drainage from a septic to a peritoneal surface does not occur, and the irregular opening produced by the "cutting out" of the suture with its accompanying delayed closure is prevented

SUMMARY AND CONCLUSION

In conclusion, the advantages of this method are

1 A comparatively small calibered tube is used, thus there is minimal encroachment upon the lumen of the bowel, yet adequate drainage is obtained because of the number of countersunk openings in the metal tip, and the uniform diameter of the lumen of the tube

2 The instrument is simple in construction as it utilizes the old principle of trocar and cannula The rubber sheath is standard size tubing and easily replaced

3 Traumatism is reduced to a minimum by avoiding clamps, mobilization in adherent segments, and "milking" of the intestine

4 Obviously, the serosal valve effect of the Witzel technique is assured, without nullifying any of the principles of modern intestinal surgery

5 By avoiding aspiration of the distended bowel and the transfixing suture, and by completely isolating the proposed point of puncture by tying the pursestring suture around the tube while the intestine is still intact, the operation may be considered "closed" and thus aseptic

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CLINICAL ASPECTS OF FIBROSARCOMA OF THE SOFT TISSUES OF THE EXTREMITIES[1]

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RECENTLY a review was made of the histories and pathological specimens in all available cases of known primary malignancy in the soft tissues of the extremities, exclusive of lymphosarcoma, malignant myeloma, and epithelioma, in which the patients had been operated on at The Mayo Clinic during the 21 year period from January 1, 1910, to December 31, 1930. There were in all 232 cases in which pathological material was available for study. Of the pathological specimens, 152 (65.5 per cent) represent fibrosarcomas. Fortunately, as a result of an efficient follow up system, there are complete data in 138 (90.8 per cent) of these 152 cases.

It is the object of this paper to present the clinical aspects, briefly discuss the pathology, review the treatment, of fibrosarcoma, and to show the final results which have been obtained for a large group of patients observed over a period of 24 years.

INCIDENCE

In addition to these 232 cases there were 13 in which a diagnosis of sarcoma was made but in which no pathological specimen was available for study. Of these, 7 were originally called fibrosarcomas or spindle-cell sarcomas. In another case, probably of fibrosarcoma, exploration was performed, but no tissue was removed for diagnosis. Finally, it is estimated that about 24 probable fibrosarcomatous tumors, some of which had been proved by previous biopsy elsewhere, were seen but were not operated on. The total number of probable and proved fibrosarcomas of the soft tissues of the extremities, encountered during this period of observation amounts to 184, an incidence of 1 in 4000 patients.

ANATOMICAL DISTRIBUTION

The larger volume of the thigh and leg, as compared with the arm and forearm, is probably the chief etiological factor that determines the more frequent development of sarcomatous tumors in the lower extremity. In two-thirds of the cases the tumors occur in this region, and 43.4 per cent of the total number are situated near the thigh or knee.

The anterior parts are somewhat more prone to be involved than the posterior, and in the upper extremity the elbow region, especially the flexor surface, is the site of predilection. Particularly susceptible is the flexor surface of the thigh, for no less than a fifth of the total number of tumors are found in this situation.

In the 152 patients there were in all 160 primary sarcomatous tumors (Fig. 1). Fifty-six occurred in the upper extremity, 104 in the lower. There were 148 patients presenting solitary tumors: the upper extremity was involved in 51 cases, or 34.5 per cent, and the lower extremity in 97, or 65.5 per cent. In 4 cases, or 2.6 per cent, true multiple sarcomas were present. In 3 (2.0 per cent) both the upper and lower extremities were involved; these however have been classified under the lower extremity, both as a matter of convenience and because this was the site of the tumor causing most concern.

GENERAL ETIOLOGICAL FACTORS

Sex. In fibrosarcoma, as in osteogenic sarcoma, males are much more frequently affected than females. Of the 152 patients, 102, or 67.1 per cent, were males and 50, or 32.9 per cent, females, a ratio of 2:1. In tumors of the upper extremity approximately one in every four patients are women, while in tumors of the lower extremity somewhat more than one in every three patients are women.

Age. Fibrosarcoma is a disease affecting chiefly those past middle life, 63 per cent of the patients with sarcoma being between the ages of 30 and 59 years. The average age incidence is 43.21 years, and the age of greatest frequency 45. 25 per cent of the patients falling in the age group between 40 and 49 years. Although no age is exempt, the least number of cases occur between the ages of

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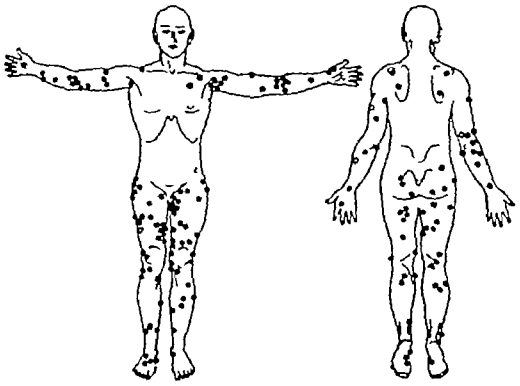

Fig 1 Diagrammatic representation of anatomical situation of 160 primary fibrosarcomas of soft tissue, which affected 152 patients The main sarcoma is represented by a solid black circle, the accessory primary sarcoma, by an outline circle.

Fig 2 Huge fibrocellular sarcoma of the thigh

10 and 15 years The youngest patient in the series was a girl, 1 month old, who presented a congenital tumor of the foot, the oldest was a man 80 years of age In 6, or 3 95 per cent of the cases, the fibrosarcoma occurred before the age of 10, whereas in 8, or 5 26 per cent, from the ages of 70 to 79 years

The average age incidence for females is slightly greater than for males, and correspondingly, the age of maximal incidence is relatively increased For males the incidence reaches its height between the ages of 40 and 45 years, for females, it closely approaches the fiftieth year

Trauma In the present series of 152 cases there were 102 in which no history of antecedent trauma was elicited In the 50 remaining, or 32 9 per cent, some type of injury preceded the appearance of the tumor In 31 of the cases there seemed to be little that would suggest more than an accidental association, however, the possibility must be borne in mind, even in these, that trauma may have been the exciting factor Five of the 31 patients gave a history of sprain or strain immediately preceding the tumor In these cases it is more likely that sarcoma was the cause, rather than the effect, of the "strain" Seventeen cases (11 2 per cent) are more convincing and are able to endure critical analysis In all, the patients gave a definite history of trauma, followed within a reasonably short time by a sarcomatous tumor These probably represent a true relationship between trauma and malignancies

Heredity Heredity seems to hold little if any position as a predisposing factor in the development of fibrosarcoma In no case in the present series was a specific history of sarcoma elicited from any other member of the family Of 135 patients whose family history was definitely recorded, 23, or 17 per cent, gave a familial history of cancer This is considerably lower than the incidence given by Deelman in a study of the occurrence of cancer in the families of 250 noncancerous persons

GROSS ANATOMY AND CHARACTERISTICS OF GROWTH

The subcutaneous and intermuscular tissues are the favorite sites for the development of fibrosarcomas (Fig 2) Frequently these tumors are found densely adherent to tendinous aponeuroses and fascial envelopes, from which they manifestly spring The cutis is a less frequent nidus, whereas occasionally an intramuscular source is clear Rarely can a definite nerve origin be demonstrated, but not infrequently nerve trunks, as well as blood vessels and other structures, are completely surrounded by the growth

These tumors are usually single, but occasionally arise primarily from multiple foci They are rounded or lobulated, and are ordinarily sharply delimited from the surrounding tissues The great majority grow expansively, the central portions increasing with the peripheral portions This process may be modified by the appearance of a multicentric form of growth, probably determined by perivascular proliferation and giving rise to tumors not unlike large, multiple uterine fibromyomas In extraordinary cases, an invasive character may be a prominent feature, the tumor

Fig 3 Huge ulcerating, bleeding fibrosarcoma, grade 4, invading bone

growing in the interstices and infiltrating the surrounding tissues.

The gross texture reflects the minute structure of the tumor The highly cellular and vascular tumors are soft and present a homogeneous appearance on section The fibrous growths are hard, non-vascular and, when cut, reveal a fasciculated architecture produced by bundles of fibrous tissue traversing various planes Edema hemorrhage, mucoid degeneration, and cyst formation may be present, particularly in the softer more cellular tumors In myxosarcoma, a soft, gelatinous, translucent structure recalls the nature of the growth

Encapsulation is a characteristic feature of a large number of fibrosarcomas, 73 of the 132 tumors for which excision or amputation was performed being encapsulated Small tumors generally have a delicate vascular investment of fibrous tissue adherent to their surfaces With larger growths the enveloping tissue is often quite thick and firmly attached to the surrounding parts Even though encapsulated, these tumors present a remarkable capacity for growing and molding themselves about structures, large arteries, veins, and nerves may be completely encased within a solid tumorous mass These tumors may penetrate their capsule absorb it, and invade surrounding tissues however a remarkable feature is the often present protective zone of fibrous tissue that is built up at the margin of the advancing tumor This inherent protective mechanism is exemplified in many cases of secondary invasion of muscle in which, on microscopic study a wall of connective tissue is seen to intervene between the healthy and involved portion of the muscle.

Bone (Fig 3) may be thinned by pressure and, not infrequently invaded and destroyed. In other instances, periosteal proliferation and cortical *thickening without actual involvement* of the bone may result from the irritation of the tumor Muscle affords a favorite soil for secondary invasion, which is present in nearly all cases in which the tumors attain sufficient size. Destruction of skin, with ulceration, was a prominent feature in 23 cases It may occur spontaneously or as the result of operative intervention, or it may occur from the application of cancer pastes

Recurrent tumors are frequently single and, like the primary growths, are usually well circumscribed frequently they are encapsulated However they may be multiple and be scattered throughout the tissues, and they may involve the *parts some distance from the original growth* although the usual site of recurrence is in the region of the previous operative incision.

MICROSCOPIC STRUCTURE AND GRADE OF MALIGNANCY

Fibrosarcoma presents a feature that constitutes a measurable indication of the normal functioning capacity of the cells, namely fibrogenesis In other tumors of connective tissue type, osteogenic sarcomas and chondrosarcomas, the same power is manifest in the production of bone and cartilage, and the relative malignancy of these tumors is dependent on the amount of bone and cartilage they produce and the degree to which these products approach the adult type In fibrosarcoma, however there is no factor to indicate the relative adultness of the matrix, except in myxosarcoma, where the gelatinous groundwork recalls an embryonic structure.

However the degree of malignancy of fibrosarcoma can be more accurately determined microscopically than for either osteogenic sarcoma or chondrosarcoma because the *structure* of fibrosarcoma is usually the same throughout the whole tumor whereas the structure of the other types not infrequently varies greatly in different parts of the same growth Consequently

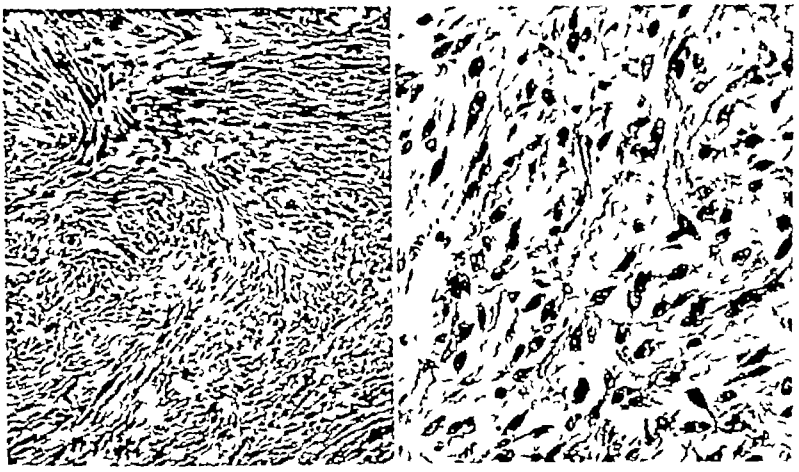

Fig 4 a, left, Fibrosarcoma, grade 1, ×125, b, fibrocellular fibrosarcoma, grade 2, ×280

considerable reliance can be placed on a given section of a fibrosarcoma, for it will usually reveal the nature of the bulk of the tumor

The microscopic grade of a tumor is an index of the degree of malignancy The customary plan of using four grades, according to the method devised by one of us (Broders), has been adopted, grade 1 indicating the lowest and grade 4 the highest degrees of malignancy The amount of fibrogenesis, the relative proportion of fibers and cells, and the amount of differentiation of the cells, form the foundation for the grading of fibrosarcomas Using these criteria, three types may be distinguished fibrous, fibrocellular, and cellular (Fig 4a)

The great majority of fibrous and fibrocellular tumors (Fig 4b) are made up of large spindle cells which approach the fibroblast type, consequently, they are more or less differentiated Their degree of malignancy is directly proportional to the number of mitotic figures and tumor giant cells which they exhibit Fibromyxosarcomas, depending on the proportion of cells and fibers, may fall in either the fibrous or the fibrocellular group The term fibrous fibrosarcoma of grade 1 means a slowly growing tumor, of a relatively low grade of malignancy, which is composed of cells closely approaching the fibroblast type and producing an abundance of collagen fibers As the grade of malignancy increases, more and more tumors fall in the fibrocellular group The term fibrocellular fibrosarcoma of grade 4 indicates a very highly malignant tumor, which exhibits numerous mitotic figures and a moderate number of collagen fibers

The highly cellular sarcomas are all extremely malignant, which is exemplified by the undifferentiated nature of the cells, by hyperchromatism of the nuclei, and by scanty fibrogenic qualities The relative number of mitotic figures is of little practical value in estimating the degree of malignancy of these tumors, furthermore, it is often misleading There were only 4 cures (7 per cent) in 57 cases, and there was absolutely no relation between the number of mitotic figures present in the tumors and the final results obtained (Fig 5)

Recurring tumors nearly always exhibit the same degree of malignancy as the previous growths, and in only a very few instances does a noticeable change take place The dictum that with each recurrence the tumor frequently becomes more and more malignant is not substantiated by the present work

For practical purposes, the fibrous and fibrocellular groups have been considered under one heading, for, as the index of malignancy increases, the fibrous group becomes replaced by the fibrocellular, thus, in grade 3, there were but 3 fibrous growths in a total of 23 tumors It has been found, however, that the relative malignancy, determined by the number of mitotic figures, decreases slightly in inverse proportion to the number of fibers

In 70, or 46 per cent, of the 152 cases the tumor was classified as grade 4, 65 of them falling in the cellular group In the combined fibrous and fibrocellular group there were 87 tumors, 35 (40 2 per cent) of which were graded 2 and only 5 graded 4

The age of greatest frequency is considerably lower among patients who are affected with cellular sarcomas than among those with fibrous and

Fig 5 Cellular fibrosarcoma

TABLE I.—DURATION OF LIFE OF 104 PATIENTS WHO ARE KNOWN TO HAVE DIED FROM THE SARCOMA

Type and grade of malignancy of tumor	Cases	Average duration of life, expressed in months from date of first operation at clinic until death	Average duration of life, expressed in months from date of symptoms until death
Fibrous and fibrocellular			
Grade	13	37 05	10 56
Grade	19	7 53	19 51
Grade 3	5	13 06	43
Grade 4	5	3	19 3
	51		67 7
Cellular			
Grade 4	53	3 8	81 9

fibrocellular tumors, the average age incidence being 36 5 and 48.2 years, respectively

CLINICAL COURSE

The clinical course of fibrosarcoma is progressive rapid or slow, depending on the structure of the tumor After local excision the disease usually recurs, and, with each recurrence involves more and more of the surrounding tissues eventually it produces metastasis, or death from exhaustion, emaciation or hemorrhage. Recurrences, as they progress in number frequently come closer and closer together occasionally there is an increase in the rapidity of growth, although usually the same structure is exhibited.

In some cases, a small benign nodule of several years duration may take on malignant change In 9 cases small tumors had been present between 7½ and 35½ years before acti e growth began Three of the tumors were of grade 1, 4 of grade 2 and 2 which were highly cellular of grade 4

Cellular sarcomas, although highly malignant usually run a longer course than the less malignant fibrocellular tumors. Thus, of 104 patients who are known to have died as a result of the sarcoma the average duration of life from the onset of symptoms until death, for the cellular and fibrous and fibrocellular types, was 81 9 and 67 7 months, respectively (Table I) Persistent recurrence after excision, and a tendency to metastasize to the lung is a characteristic feature of hyperchromatic spindle-cell tumors Probably in many of these cases the patients develop early pulmonary involvement, but, as a result of the slow progress of the disease the pulmonary implants do not become prominent until late

Pain either local or radiating, was a prominent feature in 36 per cent of the cases. Referred pain, numbness, and partial or complete palsy indicate peripheral neuritis which is the result of pressure or actual invasion, and which may antedate the appearance of the tumor

Fever leucocytosis, and anemia are not characteristically associated with fibrosarcoma, and, when present, are usually the result of secondary infection, while loss of weight suggests long standing malignancy or metastasis.

The demonstration of metastasis nearly always implies death within a few months however there was one remarkable case of a man, presenting a vascular cellular tumor of the thigh, who survived 4 years and 7 months after the development of pulmonary involvement.

Intrathoracic pressure or pain, the onset of cough and the expectoration of blood, even in the presence of a normal roentgenogram of the chest nearly always indicate pulmonary involvement

Invasion of regional or distant lymph nodes is an occasional feature of fibrosarcoma. Mediastinal, bronchial, and retroperitoneal lymph nodes are at times involved Less frequent sites of metastasis are the skull, ribs, vertebræ, subcutaneous tissues, muscles, pharynx, and brain. Of the cases in this series, there were 5 instances of involvement of regional lymph nodes 2 of these cases involved the axillary and 3 the inguinal lymph nodes Intra-abdominal metastasis, including involvement of the liver was present in 15 cases, in 13 of which the disease was primary in the lower extremity

Roentgenological examination of the parts (Fig 6) if the tumor is large, usually reveals the

Fig 6 Fibrocellular sarcoma of the arm Metastatic growths were present in the lungs, ribs, nasopharynx, and subcutaneous tissues

Fig 7 Highly cellular fibrosarcoma which recurred, showing island of bone and bone marrow Amputation was performed and 20 year cure resulted

shadow of a soft tissue which occasionally reveals areas of calcification, which may lead to the erroneous diagnosis of angioma Evidence of periosteal and cortical thickening, or actual invasion of bone is sometimes demonstrated, and was present in 28 of these cases

A most important procedure is the routine roentgenographic examination of the chest, in every case of suspected malignancy, to determine the presence or absence of visible pulmonary metastasis

TREATMENT

An estimation of the comparative value of the different methods of treatment of fibrosarcoma constitutes one of the greatest problems of surgery Small primary tumors are properly treated by wide excision, which often effects a cure In larger growths, the treatment of choice consists of excision or amputation, but the final result is dependent more upon the structure and inherent degree of malignancy of the tumor than upon any particular type of surgical procedure which aims to eradicate the disease

If amputation were performed in every case a higher percentage of cures would be realized, but if this procedure were universally adopted, it is evident that many patients would sacrifice a limb unnecessarily, of the 28 cured patients in this series, only 6 had amputation performed Amputation, on the other hand, occasionally effects a cure in cases in which excision is impossible or in which persistent recurrence demands its application The results from amputation in these types of cases, however, are not good, and of 34 cases in which there were no demonstrable signs of metastasis, and in which amputation was performed at the clinic, there were but 5 cures (14 7 per cent) Furthermore, among 21 patients, who had had only 1 previous excision, there were but 3 cures (14 3 per cent) The grade of the tumor indicates the expected results, for in only 1 of the 5 cases, in which there was no demonstrable metastasis, and in which amputation resulted in a cure, was the tumor graded 4 (Fig 7) In another case in which the tumor had been excised and graded 4, the patient had subsequent amputation performed and was cured

In cases of involvement of muscle, wide excision through healthy muscular tissue, even to the performance of myectomy, depending upon the extent of the disease, should be performed Even a group of muscles may be completely removed, and satisfactory functional results obtained In cases in which secondary involvement of the nerves is present, it may be necessary to remove partially or completely a section of an important nerve

The employment of mixed toxins of the Streptococcus erysipelatis and Bacillus prodigiosus appears to have a limited therapeutic value in the treatment of fibrosarcoma Coley's toxin may produce some softening of the tumor and, at times, visible shrinkage, we use it, however, as an adjunct to surgical treatment We have no evidence, in this study, of cure from the use of the toxin alone

Radium and roentgenotherapy have been used with some success in certain sarcomas, chiefly the round cell, lymphocytic variety and in endothelioma Fibrosarcoma, on the other hand, is a highly radioresistant tumor, though it occasionally responds somewhat favorably to radium or roentgenotherapy The general treatment which has been adopted, in appropriate cases, is excision, followed by prolonged irradiation (Seyer-

TABLE II.—SARCOMA OF UPPER EXTREMITY, RESULTS IN 44 CASES ACCORDING TO TYPE, GRADE, AND SITUATION OF LESION

	Shoulder		Arm		Elbow region		Forearm		Hand		Total		Clinical cures, per cent
	D*	C†	D	C	D	C	D	C	D	C	D	C	
Fibrous and fibro-cellular sarcoma													
Grade												3	[illegible]
Grade			3								8	5	[illegible]
Grade 3											3		[illegible]
Grade													[illegible]
				3	3		5				8	9	[illegible]
Per cent of clinical cures	[illegible]		43		16.7		[illegible]		[illegible]		[illegible]		
Cellular sarcoma													
Grade 4			7		4		5				[illegible]		3
Per cent of clinical cures	[illegible]		[illegible]		[illegible]		16.7		[illegible]		3		
	3		7	3	9			3			34	[illegible]	[illegible]
Per cent of clinical cures, total	[illegible]				[illegible]		[illegible]		[illegible]		[illegible]		

*D Dead
†C Clinically cured

lein and Hoelzel, Wollner Rostock, Hintze) In addition, Seitz and Wintz, and Quick and Cutler believe that pre-operative irradiation should also be employed. Regaud, Roux Berger and others concluded from a study of nine fibrosarcomas, *that roentgenotherapy is preferable to radium* none of their patients, however, was cured.

An intelligent evaluation of the therapeutic value of radium and roentgenotherapy in the treatment of fibrosarcoma is a very difficult problem. In the present series, the majority of patients who were subjected to excision of the tumor were given subsequent irradiation This factor together with the relatively small number of cured patients, makes the determination of beneficial results even more difficult.

An analysis of the results obtained by the different adjunctive methods of treatment, alone or in combination is difficult to evaluate. An analysis of the case histories of the cured patients reveals little of note, except that there was a predominance of sarcomas of a low grade of malignancy Of the 28 patients who were cured, 4 were treated by excision alone 1 by excision and Coley's toxin 17 by excision and radiotherapy alone, or in combination with Coley's toxin and 6 by amputation.

There are no cases in which either roentgenotherapy or radium effected a cure of a definite recurrence. Irradiation does, however occasionally produce a definite retardation of the growth of the tumor Petersen's statement, that cures of sarcoma by roentgenotherapy are possible but extraordinarily rare, is borne out by the present work. Perhaps with earlier diagnosis, larger dosage, and improved technique, roentgenotherapy may in the future, be of real benefit in the treatment of fibrosarcoma.

PROGNOSIS

The prognosis in a given case is dependent on the extent, situation, and duration of the disease its rate of progress the amount of invasion of surrounding tissues the number of previous excisions and above all, on the cellular structure of the tumor Situation, next to cellular structure, is the most important single consideration. Tumors of the lower extremity are more serious than those affecting the upper extremity (Tables II and III) and tumors of the buttock and thigh have an especially poor prognosis. Rapidity of growth usually implies a high degree of malignancy Tumors which have been excised on several previous occasions usually have an unfavorable prognosis. Of the 28 patients who were cured, a conspicuous feature was the relatively high number of instances in which previous excision of sarcoma had not been employed (14 cases).

RESULTS

Of the 132 patients who either died as the result of sarcoma or were cured (Table IV) 28, or 21.2

TABLE III—LOWER EXTREMITY RESULTS IN 88 CASES ACCORDING TO TYPE, GRADE AND SITUATION OF LESION

	Buttock		Thigh		Knee region and popliteal space		Leg		Foot		Total		Clinical cures per cent
	D*	C†	D	C	D	C	D	C	D	C	D	C	
Fibrosarcoma													
Grade 1	1	0	5	0	2	1		0	0	0	10	1	41
Grade 2	1	0	0	2	0	1	1	2	0	1	11	6	35.3
Grade 3	1	0	4	0	1	0	3	2	1	0	12	2	14.3
Grade 4	1	0	1	0	0	0	1	0	0	0	3	0	0.0
	4	0	10	8	3		7	4	1	1	36	15	29.4
Per cent of clinical cures	0.0		44.0		50.0		36.4		50.0		29.4		
Cellular sarcoma													
Grade 4		0	17	0	8	2	4	1	6	0	34	3	8.1
Per cent of clinical cures	0.0		0.0		8.1		20.0		0.0		8.1		
	6	0	36	8	10	4	11	5	7	1	70	18	20.5
Per cent of clinical cures total	0.0		18.2		28.6		31.3		12.5		0.5		

*D Died.
†C Clinically cured

per cent, were free of disease for 5 years or more Six other patients are living and either have the disease, or the period is too short to be of value in estimating the final results The 14 additional patients, which bring the total number to 152, constitute a group in which it has been impossible to obtain reliable information concerning the final outcome, many of them have died but the cause of death has been unascertainable Of the 28 patients who were cured, 24 were free of disease for from 5 to 20 years, 18 from 5 to 10 years, and 6 from 10 to 20 years

These cases, for the most part, represent a rather advanced stage of the disease There was demonstrable metastasis in 9 cases at the time the patients registered at the clinic In 20 other cases, the disease was far advanced, and biopsy alone was undertaken, the patients either refused amputation, or the situation of the tumor was such as to render its removal impossible If these 29 cases are excluded as inoperable, the final number of cures, for operable cases, amounts to 27 1 per cent This figure is extremely good, considering the length of time during which the patients were observed

Pulmonary metastasis constitutes the chief cause of the fatal termination of fibrosarcoma, and, not infrequently, arises from tumors which have a relatively low grade of malignancy Of 12 patients who had grade 1 fibrosarcoma, and who died as the result of the disease, no less than 5 are known to have developed pulmonary metastasis

SUMMARY

A review of the primary malignant tumors of the soft tissues of the extremities, excluding lymphosarcoma, malignant myeloma, and epithelioma, which were treated operatively at the Mayo Clinic in 21 years permits the study of a relatively large number of cases, 152, and a follow up of 90 8 per cent, in which the diagnosis of fibrosarcoma was made The history, the physical, laboratory, and surgical findings in these cases have been carefully studied and the pathological specimens have been examined again in order to reclassify and grade the degree of malignancy Inasmuch as the patients in these cases have been seen over a period of 24 years, and because none of these have been observed for less than 3 years, the cases have been thought to be of sufficient value to permit certain conclusions

The anatomical distribution revealed that in two-thirds of the cases, the growth occurred in the lower extremity, and that in about half of these cases, it was situated in the region of the knee

The sex incidence disclosed that males were affected twice as often as were females and the average age in this group was slightly more than 43 years, but the range was from 1 to 80 years

There was a history of trauma in 32.9 per cent of the cases in 11 per cent of these cases, there appeared to be a true relationship between the injury and the formation of the tumor

Heredity apparently had little bearing as an etiological factor no patient gave a specific family history of sarcoma, although 17 per cent gave a history of carcinoma in the family

Fibrosarcomas appeared encapsulated in 50 per cent of the cases and were usually single or lobulated and sharply defined in a layer of healthy connective tissue.

Bone was found to have been usually absorbed by pressure, but it may be invaded and destroyed.

Microscopically fibrosarcomas are uniform in structure therefore, sections removed at biopsy usually represent the true nature of the bulk of the tumor The microscopic grade is an index to the degree of malignancy, grade 1 representing the lowest grade and grade 4 the highest grade of malignancy The types of fibrosarcoma are fibrous, fibrocellular and cellular for practical purposes we combine the first two The fibrous and fibrocellular types appear at a later age than does the cellular and the latter type constitutes more than 90 per cent of growths in which the degree of malignancy was high, or grade 4.

The clinical course of the tumor unless destroyed, may be rapid or slow and there may be recurrence after treatment. Recurrence eventually produces emaciation, exhaustion metastasis, or hemorrhage and death. The roentgenogram reveals the first indication of pulmonary metastasis in the extremity the tumors cast a shadow which at times may be clearly outlined.

Treatment of the smaller tumors should consist of wide excision whenever possible. Surgical removal of large tumors may be impossible and amputation of the part may be necessary Others are so situated as to make surgical treatment of little more than diagnostic value and many tumors, which appear inoperable, have at biopsy proved to be of a low degree of malignancy and curable.

Irradiation alone has been resorted to in cases in which tumors could not be removed by excision or amputation or in which the patient refused surgical treatment Postoperative irradiation has, however been used, and no doubt causes a delay in recurrence It is difficult to evaluate the therapeutic benefits and, no doubt, with increased knowledge as to the dosage and improved technique, a more definite value as to the pre-operative and postoperative influence on the growth of fibrosarcomas will be arrived at. Our experience would indicate that these tumors are highly radioresistant and we are of the opinion that operation offers the more favorable result. The prognosis is chiefly dependent on the structure of the tumor and on the degree of malignancy The more malignant the tumor the more radical should be the treatment. Early amputation would result in more cures than are obtained otherwise, but the surgeon and the patient resort to it only after conservative measures fail The proper co-operation of the surgeon, the pathologist, and the patient are essential for the best results

TABLE IV —RESULTS OF TREATMENT IN 132 CASES IN WHICH THE PATIENTS EITHER DIED AS THE RESULT OF SARCOMA OR WERE CURED[1]

Type and grade of malignancy of tumor	Cases	Clinically cured	Dead	Cured clinically per cent
Fibrous and fibrocellular				
Grade	[illegible]	[illegible]		43
Grade	30		[illegible]	[illegible]
Grade 3	18	2	13	[illegible]
Grade 4	5		5	[illegible]
	73	54	3	[illegible]
Cellular				
Grade 4	37		33	7
Total	32	48	[illegible]	[illegible]

All of the 48 cures with the exception of 4, have persisted more than 5 years One patient has been free from symptoms for 3 years and 8 months, patients for 4 years and 8 months and patients for 4 years and months In all probability all of these patients will pass the 5 year period Another patient has been free of symptoms for 3 years

We feel that microscopic examination of the tumor, in order to determine the type and degree of malignancy is of great value in determining the type of surgical treatment advisable in each case The surgeon, in determining the prognosis, must consider the site, size, duration, and rapidity of growth the invasion of important structures, such as nerves and blood vessels previous treatment, and pathological findings. Pulmonary metastasis is the most common cause of death and may occur in cases in which the grade of malignancy is relatively low Nine patients revealed pulmonary metastasis at the time of their admission to the hospital. Twenty patients revealed evidence of advanced disease and biopsy alone was performed

In our series of 132 patients, 28 (or more than 21 per cent) lived for 3 years following excision or amputation 24 patients (17 5 per cent) survived 5 to 20 years 18 patients (14 4 per cent) survived 5 to 10 years, and 6 patients (4 5 per cent) survived 10 to 20 years

If we exclude the 29 cases in which the lesion was considered inoperable, or in which the patients refused operation, it is found that in 27.1 per cent of the cases, the patients survived for 3 or more years after the operation.

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EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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JUNE 1936

THE MECHANISM OF THE VERMIFORM APPENDIX—A POTENTIAL CLOSED-LOOP"

THE alleged causes of appendicitis are multiple Only two however have survived the crucial test of experimental inquiry viz infection and obstruction Efforts directed at the establishment of the pathological picture of appendicitis in the cecal appendage of the dog have shown that these two factors must invariably be concurrently present in order to produce the disease [1] High grade obstructions of the cecal appendage in the dog when specific pyogenic organisms or feces are present in the lumen, are regularly attended by a process akin to that observed in appendicitis when the lumen of the cecal appendage is washed obstruction is not attended by significant consequence The presence of pathological organisms without obstruction is equally well borne.

The investigations of Professor Aschoff[2] have lent the impression that appendicitis is essentially a specific bacterial disease after the manner of gonorrhea. He finds an enterococcus more specifically a diplococcus type B lurking normally in the distal one-third of the appendix uncontaminated in the main by the more sociable organisms in the mixed flora of the proximal two-thirds When acute suppuration supervenes, the diplococcus is *found to be the predominant organism* The item of obstruction he considers as being of no importance.

In 1846 in an admirable paper too little known Adolph Volz[3] relates the significance of appendiceal concretions for perforations of the appendix When Fitz[4] in 1886 made the pronouncement that pentyphlitic suppurations were caused by disease of the vermiform appendix, his words fell upon attentive ears. In a postmortem series of 152 instances of suppuration about the cecum Fitz found an appendiceal concretion or foreign body present in 59 per cent of the cases Van Zwalenburg[5] in 1904 and Wilkie[6] in 1914 reiterated faith in the belief that obstruction was a factor of major consequence for the occurrence of appendicitis. The force of the expressions

[1] Wangensteen, O H and Bowers W F An experimental study of the significance of the obstructive factor in the genesis of acute appendicitis J Western Surg Ass 1935

[2] Aschoff L Die appendicitische Anfall, seine Anatomie und Pathogenese Berlin und Wien Julius Springer 1924

[3] Volz, A Die durch Luftblasen bedingte Durchlöcherung der Wurmfortsatzes die häufig vorkommende Ursache eines Gallenblasen Pus [illegible] und deren Behandlung mit Opium Laudanum Chr Fr Mallon [illegible] Hallensis 1846

[4] Fitz R H Perforating inflammation of the vermiform appendix with special reference to its early diagnosis and treatment Am J M Sc 1886, 92 321

[5] Van Zwalenburg C F Obstruction and consequent distension, the cause of appendicitis as proved by clinic and by experimental appendicitis in dogs J Am M Ass 1904, 42 [illegible]

[6] Wilkie D P D Acute appendicitis and acute appendicular obstruction Brit M J 1914 [illegible]

of Professor Aschoff have, however, served to minimize the purport of obstruction and have lent increased credibility to the infection factor

In describing perforation of the appendix in 1847, Gerlach[7] called attention to a mucosal fold which he described as a valve, interfering with emptying of the appendix The existence of such a valve or of a sphincter has, however, been discredited by anatomists That something of the nature of a sphincter-like mechanism uniformly exists at the base of the appendix, the writer has been able to demonstrate to his own satisfaction In a series of many cases, in which the appendix was removed as an incident during another operation or in the interval when uninflamed, a needle attached to a column of water, was inserted into the lumen of the appendix at its distal tip Resistance to the inflow of water into the cecum was consistently encountered—gravity pressures of 30 to 106 centimeters of water being withstood In 17 instances, the mean pressure which was necessary to cause water to run into the lumen of the cecum was found to be 60 centimeters of water and the average was 56 centimeters In instances in which appendectomy was done for acute suppurative appendicitis and a fecolith was found impacted in the lumen, attempts were made upon the excised appendix to dislodge the obstruction by the same means Displacement of concretions by gravity pressure on the whole was found to be difficult Rupture of the gangrenous wall by pressures in the range of the mean were not infrequent

In two appendicostomies coincidentally done together with colostomy for cancer of the bowel, opportunity has been afforded during convalescence to measure the resistance to the inflow of water under the force of gravity In both instances, the observed sustained pressure was found to be of the order of magnitude of the mean pressure noted in the acute determinations made during the course of appendectomy Attempts at influencing with drugs the obstruction to the inflow of water through an appendicostomy have lent the impression that this resistance may be enhanced or diminished through such an agency These observations made with the co-operation of my colleagues, Drs W P Ritchie and R Buirge, will be reported in detail elsewhere

Those familiar with the potential hazards of experimentally closed intestinal loops will appreciate the latent danger inherent in this mechanism In it one immediately sees an explanation for the stasis which gives rise to the formation of appendiceal concretions These are laminated and usually free from bile pigments or biliary derivatives, though they have as a rule a small nucleus which comes from the intestinal canal These concretions are found in most instances of perforative types of appendicitis In the absence of an appendicolith, the mechanism which interferes with satisfactory evacuation may also initiate the changes which give rise to suppuration Blood is pumped into the terminal arteries of the appendix under the motive force of systolic blood pressure, increase in intraluminal tension through the agency of physiological obstruction at the base of the appendix, precludes return of blood through the veins Maintenance of this pressure-tension disturbance results in a struggle for hydraulic equilibrium Rupture of venules occurs with resulting hemorrhage into the wall of the appendix Oxygenation of the tissue suffers and the mucosa loses its miraculous ability to repel invasion of bacteria from the appendiceal lumen Having been put in motion, this sequence of events can be arrested

[7]Gerlach L. Beobachtung einer toedliche Peritonitis als Folge einer Perforation des Wurmfortsatzes. Ztschr f Rat. Med. 1847, 6 12

only by the obstruction giving way The unusually generous distribution of lymphoid tissue beneath the mucosa and submucosa of the appendix is probably an important factor in determining the character of the inflammation which follows.

Man gives little promise of outgrowing this bad anatomical plan of the vermiform appendix. It appears most likely that the minute anatomy of the appendix is of more consequence than diet latitude longitude, or related factors in provoking the occurrence of appendicitis. If the obstructive mechanism at the base of the appendix, which makes of this narrow tubular viscus a potential closed loop proves to be a sphincter the significance of nervous influences becomes at once apparent. This little sword of Damocles always holds out a threat. Indications for its removal must not be too inflexible.

OWEN H. WANGENSTEEN

THE GENTLE HANDLING OF CANCER

CELLS are carried from a cancer to distant parts of the body where they multiply and give rise to foci of new cancer growth. These cells are transported by the lymphatic current or the blood stream or by both in turn.

The lymph glands interposed along the course of the lymph vessels, which drain the region of the primary focus of cancer act as filters of the lymph stream flowing through them. Cells whisked off the primary growth lodge in the meshes of this lymph gland filter When a number of cancer cells are suddenly carried into a gland by the lymph flow some of them may escape and continue on with the lymph flow to be emptied into the subclavian vein.

Microscopic examination of the tumor is the only test we can use to learn whether the cancer in question belongs to the more malignant type or not.

The more the microscopic picture of a cancer resembles the normal gland in which it arises the more closely the cells cling to the framework structure of the tumor Hence metastasis from this type of growth is delayed. On the other hand if cancer cells are less differentiated into a structure resembling the normal gland and approach more the embryonic type of cells, then the more easily are they dislodged and carried off from the mother cancer

Therefore, it behooves us in handling a tumor e g., of the breast, to be as gentle with our hands as possible lest we by roughness dislodge some cancer cells and hence be an accessory in causing distant metastasis.

If a microscopic examination of the tissue in question is necessary to establish the diagnosis, the method of obtaining this specimen must be carefully planned.

In a breast lesion it is better to excise the mass with a generous bit of the surrounding normal tissue or remove the whole breast if necessary rather than cut into the tumor

Trauma of the tumor itself by knife or needle is best avoided. Immediate cauterization of the biopsy wound in a tumor is merely locking the stable door after the horse is stolen. The location of the lesion, e g a prostatic or bronchial cancer may necessitate a biopsy to establish a diagnosis. Biopsy handicaps the patient we hope to cure. One can readily see how tissue damage opens up both the lymphatic and blood vessels as well as dislodges cancer cells that may be carried elsewhere in the body

In handling the mass in a breast we wish to learn whether there is fat atrophy over the lump whether there is skin dimpling on displacing the breast its consistency whether it is cystic and whether it shades off into normal

breast tissue or is sharply marked off from the surrounding breast If the examiner has these points consecutively in mind and decides each in its turn then the necessary handling can be reduced to a minimum It is not just to the patient to have students palpate a breast cancer More of these poor women will survive if the class practices palpation on benign breast tumors

The practical application of these principles starts when a woman with a lump in her breast presents herself for examination Let the examining hands touching the questionable lesion be as few and gentle as possible At operation the field is sterilized with the utmost gentleness The operation is done by sharp dissection Gentleness is our aim Blunt dissection or gauze wiping is avoided entirely Hemostasis is absolute It would be interesting to see how many more 5 year cures would result if such methods were universally followed.

HARRY G SLOAN

MEMOIRS

C JEFF MILLER

ON March 21 1936 America lost one of her most distinguished surgeons and magnetic personalities in the death of Dr C. Jeff Miller Dr Miller a true son of the South, represented the ultimate in medicine the science of which was greatly benefited because of his having lived. In addition to his professional attainments probably no physician ever meant as much to a community either locally or regionally in a non-professional way than Dr Miller His intense interest in the welfare of humanity is illustrated by the fact that he repeatedly took time from his busy teaching and clinical activities to head Community Chest Drives and other similar movements. Not only was his surgical judgment unsurpassed but also his broad vision and keen insight made his presence on many lay boards of inestimable value.

Dr Miller's education was that of the greatest scholar as, in addition to his profound knowledge of medicine, he was a connoisseur of music, literature, and art. Some of his happiest hours were spent in his library engrossed in J M Barrie Robert Burns, Osler and Moynihan.

As a teacher he was unsurpassed primarily because of his profound knowledge of the subject and also because of his lucid and superb presentations. Even during the most trying operative procedures he lectured clearly and his operative clinics were always filled to their maximum capacity

His ability as an executive is exemplified by the organization of his own departments and the great influence he exerted on the many boards on which he served. Often after many hours of heated controversy in which he took no part the question would be quickly settled by his logical deductions.

Those who knew Dr Miller could understand the devotion of his patients with whom he shared so freely his wise and generous counsel. He always imparted comfort and reassurance to patient and family in the soft tones of his modulated voice.

Dr Miller was born on February 9, 1874 in Winchester Tennessee, the son of Charles J and Elizabeth Johnston Miller He attended and was graduated from the University of the South, Sewanee Tennessee. His early ambition to study medicine was undoubtedly kindled during his stay with his uncle, Thaddeus Johnston, a country physician He received his M D degree from the University

C. Jeff Miller

of Tennessee in 1893 and interned at the Nashville City Hospital in 1894 On January 30, 1896, he married Ada Parker, of Memphis, Tennessee, and in 1912 their only daughter, Elizabeth, was born From 1899 to 1904 he served as chief of clinics at the Charity Hospital, New Orleans, under Dr Ernest S Lewis In 1911 Dr Miller became professor of gynecology at Tulane University, which position he held until his death He was chief of the Gynecological Services at the Charity Hospital and Touro Infirmary, New Orleans

Dr Miller was officer of many organizations He served both as secretary and as president of the Orleans Parish Medical Society From 1926 to 1936 he was a member of the Board of Regents of the American College of Surgeons and was president in 1930–1931, in 1912 he was chairman of the Section on Obstetrics, Gynecology, and Abdominal Surgery of the American Medical Association, president of the Gynecological Club in 1927, president, American Gynecological Society, 1928–1929, president of the Southern Surgical Association in 1922, president of the Southeastern Surgical Congress in 1936, and president of the Howard Memorial Library, New Orleans During the World War Dr Miller was a Major in the Medical Corps

In June, 1930, he received the honorary degree of Doctor of Science from his Alma Mater, Sewanee He was author of two textbooks, *An Introduction to Gynecology* and *Clinical Gynecology* as well as of innumerable articles on scientific subjects

Dr Miller was truly a Southern gentleman and in every way typified Jeffersonian principles He had the pioneering instinct of Lister, the judgment of Solomon, the technique of Halsted, the tenderness of Florence Nightingale, the perceptive powers of Osler, the determination of Noguchi, and practiced the ethics of Hippocrates

ALTON OCHSNER

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE small volume by Woods[1] of less than 200 pages is designed to strike a happy medium between what a specialist should know and what is essential to the general practitioner in handling the average run of otitic problems. Consequently, long treatises on otologic problems and detailed anatomical description are purposely omitted.

The illustrations are mostly drawn from life, and on the whole are very good reproductions of pathological conditions.

Having in mind the various problems confronting the general practitioner, the text is practically limited to pyogenic manifestations, and no mention is made of deafness or other otologic problems. There is a good chapter on differential diagnosis of intracranial complication.

The book undoubtedly will be found useful to men in general practice and to medical students.

J F Dreer.

A Glasgow Manual of Obstetrics[2] edited by S. J Cameron, is the second edition of this work, the first having been published in 1924 It is, on the whole, an excellent compilation. An increasing number of teachers and students believe that less padding would improve textbooks. To them the 600 pages of this manual will be a case in point. Except for a rare exception, the illustrations are all line drawings.

The text is completely up to date. The chapter on ovarian and pituitary hormones, though it is short, treats the subject fully and accurately The discussion of anesthesia considers separately drugs which alleviate pain but do not produce unconsciousness, those which produce only an amnesia, and those which result in complete unconsciousness. The use of chloroform put up in so minim pieces which can be crushed in a handkerchief for the relief of second stage pain is a suggestion worthy of trial on patients delivered in their homes in this country

Inasmuch as this manual represents the practice of those associated with the Royal Maternity of Glasgow it may be well to point out that many of their practices are quite out of favor in this country This may be accounted for in a measure by their large percentage of home deliveries Nevertheless the treatment of placenta previa by plugging the vagina with wet cotton pledgets has few supporters here, though it is only fair to say that the authors recommend cesarean section whenever there is no contra-indication. Likewise the removal of the placenta in cases of advanced abdominal pregnancy is rather generally frowned on in this country because of the frequency of uncontrollable hemorrhage. Nor do we feel justified in the use of the hot intrauterine douche for the control of postpartum hemorrhage. The use of sweats in the treatment of pre-eclamptic toxemia has very little acceptance here. The authors are to be commended for their advocacy of prompt emptying of the uterus in any form of toxemia which does not respond rapidly to other treatment.

It is unfortunate that this book will not be widely accepted in this country because of the failure of the English speaking peoples to agree on a common nomenclature for scientific work.

J E Fitzgerald.

THE unique book[3] by Harrison differs from most X-ray texts in that it is essentially a clinical presentation, taking up the human body by systems, and giving a discussion of both the diagnostic and therapeutic phases of roentgenology in relation to each The illustrations are excellent and adequate, considering that the author has limited himself to a single volume.

Special stress is laid upon the need of close association between the radiologist and the referring physician The utmost information can be obtained from the roentgen study only when the utmost information regarding the suspected pathological condition is considered in planning the examination Every roentgenological examination is an attempt to solve a definite clinical pathological problem. It should not be undertaken as a foraging expedition. Roentgen investigation is a clinical procedure and roentgen therapy is a clinical treatment. They differ essentially from laboratory tests which are concerned primarily with the examination or treatment of something which is no longer an integral part of the patient The co-operation between the clinician and the roentgenologist must be sufficiently close to ensure that the patient receives the utmost benefit from the examination. If the information supplied by the clinician is vague and incomplete,

[1] Otitis Medical Publications Patient in Hospital Diseases of the Ear. Text Book for Students and General Practitioners. By R. R. Woods, M.B F.R.C.S. London Oxford University Press, 1936.

[2] A Glasgow Manual of Obstetrics. By Samuel J. Cameron, M.B F.R.F.S F.C.O.G. John Hewitt, M.B Ch.B F.C.O.G. Robert A Lyman, M.D F.R.F.S F.C.O.G. Elias D. Marson, M.B Ch.B M.C.O.G. Med London Edward Arnold & Co. 1936

[3] A Textbook of Roentgenology. The Roentgen Ray Diagnosis and Treatment. By Rudolf J. Michael Harrison, M.B Ch.M B.M.R.E (Cantab.), F.A.C.R. Baltimore Williams & Wilkins Co. 1936.

the analysis of the roentgenological findings made by the roentgenologist must also be vague and incomplete, and to enable the patient to obtain the best possible advice indefiniteness must be replaced by accuracy These are principles which the author has set forth in the introduction to his work and they have served as a guide to him consistently throughout the entire book It deserves a wide circulation and close study JAMES T CASE

ALTHOUGH only a year has passed since the publication of the first edition of *The Radiology of Bones and Joints*[1], Brailsford presents the second edition in which supplementary material has been added Certain chapters, e g, those dealing with osteochondritis, bone dystrophies, and spondylolisthesis, have been rewritten A chapter dealing with dental radiography has been included

The volume is divided into two parts (1) "Regional Radiography," and (2) "General Discussion on Bone Changes in Systematic and Localized Disease." Due to the fact that the findings are considered regionally, there are of necessity repetitions of material covering certain bone conditions The subject matter is well illustrated Throughout the volume are found frequent references to monographs and articles dealing with the particular condition under discussion The bibliography at the end of the volume covers 18 pages

The material covered in the volume of 571 pages includes the rare as well as the more common acquired and congenital bone conditions The author's discussions of the various conditions are concise but cover the essential roentgen findings

Part II, covering 83 pages, consists of a general discussion of bone changes in systematic and localized disease The author draws freely from the available literature

The volume should prove to be a valuable addition to the reference library not only of the radiologist and surgeon, but also the general practitioner who does not claim to be a specialist but who often encounters unusual, puzzling bone conditions

EARL E BARTH.

IN his book, *A Textbook of Obstetrics*[2], Dr Irving seems to have made a definite step toward the simplification of obstetrical teaching In the introduction, he states that the book is "designed as a simple and concise textbook for students and practitioners " Furthermore this textbook is an outgrowth from the notes and outlines which have been used for obstetrical teaching in Dr Irving's department for several years

There are certain fundamentals in obstetrics that are rather definitely and generally agreed upon by those who are teaching and (or) specializing in this art This applies chiefly to normal obstetrics, i e, anatomy and physiology of the reproductive organs both in the pregnant and non-pregnant state There are certain other phases of the female organism in which our knowledge is much more limited and in which there is considerable diversity of opinion and interpretation Endocrinology is the number one of this category Therefore, any statements contained in a textbook on this phase of the subject may have to be revised a year hence Dr Irving has presented an excellent résumé of this subject in its relation to the physiology of the female reproductive function, without speculation

In the matter of pathological obstetrics we are more likely to encounter a greater diversity of opinion among those engaged in its teaching The difference is usually that of method of treatment of a given condition, and for the most part is relatively unimportant In this part of the book, a conservative attitude is maintained throughout

The book is well illustrated and a bibliography at the end of each chapter will be helpful to anyone who wishes to do more extensive reading on that particular subject There are only 550 pages in this volume which makes the book of practical size for student's use The contents are arranged in logical order, and one finds it easy reading, clear and concise CHESTER C DOHERTY

THE book by Shelling[3] on the parathyroids in health and disease is an excellent monograph The text is filled with references The chapter on hyperparathyroidism, for instance, is followed by a bibliography and 174 articles, that on hypoparathyroidism by 177 Furthermore, this represents a new review of the literature to date, it is not a revision of an old work

The normal and pathological anatomy of the parathyroids is adequately presented, there is a good description of the cell types found in the normal and hyperplastic gland The physiological review is written in the light of the author's own research The clinical discussion of hypoparathyroidism and hyperparathyroidism occupies about one-half of the book Mistakes in diagnosis and treatment of calcium deficiency states are explained In this a tabulation of differential diagnosis is helpful. The therapeutic use of parathyroid hormone is critically analyzed An appendix gives the mineral and caloric values of test diets to be used in the study of questionable cases

This monograph will be of value to both the surgeon and the internist in the diagnosis and treatment of parathyroid disease PAUL STARR.

THE fourth edition of von Jaschke's textbook[4] of obstetrics is dedicated to the late Otto Pankow to whom the author acknowledges his indebtedness for much new material on the biology and pathology

[1] THE RADIOLOGY OF BONES AND JOINTS By James F Brailsford M.D (B'ham), M.R.C.S (Eng) 2d ed. Baltimore William Wood & Co., 1935

[2] A TEXTBOOK OF OBSTETRICS FOR STUDENTS AND PRACTITIONERS By Frederick C. Irving, A.B, M D, F.A C.S New York The Macmillan Co 1936

[3] THE PARATHYROIDS IN HEALTH AND DISEASE By David H Shelling, B Sc., M.D St Louis The C V Mosby Co, 1935

[4] LEHRBUCH DER GEBURTSHILFE By Dr Rud. Th v Jaschke 4th ed Berlin Julius Springer, 1935

of pregnancy This chapter has been rewritten to include the conception of the hormonal influence in the sex cycle

The text is primarily didactic and is ample in its scope. It is printed on good paper and is rather profusely illustrated with halftones, diagrams, beautifully colored plates, and unusually clear roentgenograms.

Modern methods of diagnosis and treatment prevail for the most part, but the illustration and description of the monaural stethoscope (p. 94) *for the detection of fetal heart tones typify the* author's adherence to an outmoded method. The head-piece stethoscope, acclaimed universally in this country for two decades, is not mentioned.

Ample bibliographies are appended, containing, however, chiefly German references, few American authorities are cited

Although a good book for reference, it will *probably be in small demand in this country chiefly* because at the present rate of exchange the cost of the unbound volume is $18.00 a price indeed out of proportion to the excellent American and English texts covering the same field. *Irving F Stein*

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender Selections will be made for review in the interests of our readers and as space permits.

American Martyrs to Science through the Roentgen Rays. By Percy Brown, M D F A C.P., F A C.R. Springfield, Illinois, and Baltimore, Maryland Charles C. Thomas, 1936.

Time of Ovulation in Women; a Study on the Fertile Period in the Menstrual Cycle By Carl G Hartman Baltimore The Williams & Wilkins Co 1936.

Parenteral Therapy; a Ready Reference Manual of Extra-Oral Medication for Physicians, Dentists, Pharmacists, Chemists, Biologists, Nurses, Medical Students and Veterinarians By Walter Forest Dutton, M.D and George Burt Lake, M D Springfield, Illinois, and Baltimore, Maryland Charles C Thomas, 1936

Fotografia del estomago sus aplicaciones en el diagnostico del cancer del estomago By Dr Herbert Hofmann Buenos Aires Ancelo Lopez, Imp , 1936

Surgical Emergencies in Children. By Harold Clifford Edwards, M S (Lond) F R.C.S (Eng). Baltimore William Wood & Co 1936

Physiopathologie des operations sur le foie et les voies biliaires le mécanisme des accidents By Raoul Gerding Palmer Paris Librairie E. le François, 1934

Neurological Surgery. By Loyal Davis, M.S , M D., Ph.D D Sc. (Hon). Philadelphia Lea & Febiger, 1936.

The Balanced Diet. By Logan Clendening, M D New York and London D Appleton Century Co 1936

Pathologie und Klinik der Eierstockgeschwülste. Edited by L. Aschoff, H Elias, H. Eppinger, C. Sternberg, K. F Wenckebach Band vii. Die gutartigen Kleinzysten By Prof. Dr F de Quervain and Prof. Dr C. Wegelin Berlin and Vienna Julius Springer, 1936.

Obstetrical Practice By Alfred C. Beck, M D. Baltimore The Williams & Wilkins Co , 1934.

Handbook of Surgery. By Eric C. Makin, M B Ch B F R C.S (Edin) With a foreword by John Fraser, M C , M D Ch M., F.R C.S E. Baltimore. William Wood & Co 1936

Emergency Surgery By Hamilton Bailey F R C.S (Eng) 2d ed. Baltimore William Wood & Co , 1936

The Intervals By Arthur Grollman, Ph D M D Baltimore The Williams & Wilkins Co 1936.

Medizinische Praxis, Sammlung für ärztliche Fortbildung. Edited by Prof Dr L. R. Grote, Prof Dr. A Fromme and Prof. Dr K. Wamekros Vol ix—Blutarmut und Fieber By Prof. Dr. Hans Runge Dresden and Leipzig Theodor Steinkopff, 1936

The Practitioners Library of Medicine and Surgery Vol. x—Dermatology and Syphilology New York and London D Appleton-Century Co 1936.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

DAVID C BARROW, Rochester, *President* EUGENE H POOL, New York *President-Elect*
HENRY P BROWN, JR, *Chairman* GILSON C ENGEL, *Secretary, Committee on Arrangements*

PRELIMINARY CLINICAL PROGRAM FOR 1936 CLINICAL CONGRESS

FOR the twenty-sixth annual Clinical Congress of the American College of Surgeons to be held in Philadelphia, October 19-23, 1936, the surgeons of that great medical center have organized under the leadership of a strong and representative committee They plan to provide a program of surgical clinics and demonstrations that will present a complete showing of their clinical activities in all departments of surgery The committee is assured of the hearty co-operation of the clinicians at the five medical schools and more than thirty hospitals that will participate in the clinical program

The Executive Committee in charge of arrangements is as follows Henry P Brown Jr, chairman, Gilson C Engel, secretary, Francis H Adler, Dorothy C Blechschmidt John O Bower L K Ferguson, Bruce L Fleming, Karl M Houser Robert H Ivy, H P Leopold, Richard H Meade, Jr, Francesco Mogavero, John R Moore, L A Mullen and Lewis C Scheffey

A preliminary schedule of such clinics and demonstrations appears in the following pages Published in tentative form, and incomplete as to the participating hospitals, the clinical program is to be revised and amplified during the coming months as the work of the program committee progresses It will be noted that operative clinics and demonstrations in the hospitals are scheduled for the afternoon of Monday, October 19, beginning at 2 o clock, and for the mornings and afternoons of each of the four following days The real program of the Congress will be published from day to day—a complete and accurately detailed program being posted in the form of bulletins at headquarters each afternoon for the succeeding day and issued in printed form the following morning All departments of surgery will be represented therein—general surgery, gynecology and obstetrics, genito-urinary surgery, neurosurgery orthopedics, surgery of the eye, ear, nose and throat

The following hospitals will participate in the clinical program Abington, American Oncologic, Broad Street, Bryn Mawr, Chestnut Hill, Children s, Children's Hospital of the Mary J Drexel Home, Cooper (Camden), Delaware County, Episcopal, Fitzgerald-Mercy, Frankford, Germantown, Graduate Hospital of the University of Pennsylvania, Hahnemann, Hospital of the University of Pennsylvania, Hospital of Woman's Medical College, Jeanes, Jefferson, Jewish, Kensington, Lankenau, Memorial, Methodist Episcopal, Misericordia, Mount Sinai, Northeastern, Pennsylvania Philadelphia General, Philadelphia Orthopedic, Presbyterian, St Agnes, St Christopher s St Joseph's, St Luke's and Children's, St Mary's, St Vincent's, Shriner's, Stetson, Temple University, Wills Eye, Woman's

The committee is planning to develop many special features in the clinical program including among other features (1) Cancer clinics demonstrating the treatment of cancer by surgery, radium and X-ray, (2) fracture clinics demonstrating modern methods in the treatment of fractures, (3) clinics in traumatic surgery for the presentation of the newer methods of rehabilitation of the injured by surgery and physical therapy

In addition to an extensive schedule of operative clinics and demonstrations at the hospitals, the subcommittee on ophthalmology and otolaryngology is preparing a series of clinical demonstrations to be given by visiting ophthalmologists and otolaryngologists, to be presented each forenoon at the headquarters hotel

EVENING MEETINGS

Programs for the five evening scientific sessions, to be held in Irvine Hall, are being prepared by

the Executive Committee of the Board of Regents. At the presidential meeting on Monday evening, the first formal session of the Congress, the retiring president, Dr Donald C. Balfour will deliver his address. At this session the new officers will be inaugurated Dr Eugene H. Pool, New York, president Dr Emile Holman, San Francisco, first vice-president Dr George E. Wilson, Toronto second vice-president.

At the annual Convocation of the College on Friday evening the 1936 class of initiates will be received into Fellowship. On this occasion Dr Eugene H. Pool will deliver the presidential address. At sessions on Tuesday Wednesday and Thursday evenings eminent surgeons of the United States and Canada, together with a number of visiting surgeons from foreign countries, will present and discuss papers dealing with surgical subjects of timely importance.

It is expected that at this year's Congress we will be honored by the presence of a number of distinguished European surgeons. Among those who have indicated that they will attend are the following Sir James Walton, London, England Dr William Fletcher Shaw Manchester England Archibald Hector McIndoe, London, England Dr Alexander MacLennan Glasgow Scotland Prof. Dr Paul Chaimont, Zurich, Switzerland Prof Dr. Martin Kirschner Heidelberg, Germany Prof. Wolfgang Rosenthal, Leipzig, Germany and Prof. Dr F Sauerbruch, Berlin, Germany

SPECIAL FEATURES OF THE PROGRAM

Special features of the program for this year's Congress include (1) A conference on fractures under the auspices of the Committee on the Treatment of Fractures (2) a symposium on cancer arranged by the Committee on the Treatment of Malignant Diseases, (3) a conference on industrial medicine and traumatic surgery under the auspices of the Committee on Industrial Medicine and Traumatic Surgery

The showing of surgical motion pictures demonstrating clinical features of interest, has met with popular acceptance in recent years and will be continued at this year's Congress with an enlarged program of films, both sound and silent, to be exhibited daily at headquarters

Following its established custom and in recognition of an obligation to the public to provide authoritative information on modern surgery better hospitals and the prevention of disease, a community health meeting will be held on Wednesday evening under the auspices of the College in the Municipal Auditorium.

HOSPITAL CONFERENCE

The annual hospital conference will open the Congress with a session in the Rose Garden of the Bellevue-Stratford Hotel at 10 o clock on Monday morning An interesting program of papers, round table conferences, and practical demonstrations dealing with problems related to hospital efficiency is being prepared for sessions on Monday Tuesday Wednesday and Thursday A greatly increased interest on the part of surgeons in both the administrative and scientific phases of hospital work has been evidenced in recent years and the program for this year's conference will provide for discussions of subjects of interest to the three major hospital groups—medical, surgical, and administrative. It is proposed to make this year's program of wide interest and practical character through a careful selection of subjects to be presented and discussed by surgeons and hospital executives, particular emphasis being directed toward professional standards and the vital problems related to hospital economics.

HEADQUARTERS—TECHNICAL EXHIBITION

Clinical Congress headquarters will be established at the Bellevue Stratford Hotel, which has unusual facilities for accommodating the Congress. The grand ballroom, Garden, Clover and Red Rooms and other large rooms on the first and second floors and the roof have been reserved for scientific sessions and conferences, registration and clinic ticket bureaus, bulletin boards, executive offices, etc. Thus, the activities of the Congress will be centralized under one roof.

The Technical Exhibition will be located in the ballroom and adjacent large rooms on the second floor The registration and clinic ticket bureau together with the registration desk will be centrally located as regards the exhibit rooms, in which will be placed the bulletin boards on which the daily clinical program will be posted each afternoon. Leading manufacturers of surgical instruments and supplies, X-ray apparatus, operating room lights, hospital apparatus and supplies of all kinds, ligatures, dressings, pharmaceuticals and publishers of medical books will be represented in this Exhibition.

ADVANCE REGISTRATION

The hospitals and medical schools of Philadelphia afford accommodations for a large number of visiting surgeons, but to insure against overcrowding, attendance at the Congress will be limited to a number that can be comfortably accommodated at the clinics—the limit of attendance being based upon the result of a survey of the

amphitheaters, operating rooms, and laboratories of the hospitals and medical schools to determine their capacity for visitors. It is expected, therefore, that those surgeons who wish to attend the Congress will register in advance.

Admittance to all clinics and demonstrations will be controlled by means of special clinic tickets, which plan provides an efficient means for the distribution of the visiting surgeons among the several clinics and insures against overcrowding, as the number of tickets issued for any clinic will be limited to the capacity of the room in which that clinic will be given.

A registration fee of $5.00 is required of each surgeon attending the annual Clinical Congress, such fees providing the funds with which to meet the expenses of the meeting. To each surgeon registering in advance a formal receipt for the registration fee is issued, which receipt is to be exchanged for a general admission card upon his registration at headquarters. This card, which is non-transferable, must be presented in order to secure clinic tickets and admission to the evening meetings.

PHILADELPHIA HOTELS AND THEIR RATES

In addition to the headquarters hotel, the Bellevue Stratford, there are several first-class hotels within short walking distance of headquarters providing ample hotel facilities at reasonable rates. It is suggested that reservation of hotel accommodation be made at an early date. The following hotels are recommended by the Committee:

	Minimum Rate with Bath	
	Single	Double
Adelphia, 13th and Chestnut Sts	$3.50	$5.00
Barclay, Rittenhouse Square, I	4.00	6.00
Belgravia, 1811 Chestnut St	2.50	4.00
Bellevue-Stratford, Broad and Walnut Sts	4.00	6.00
Benjamin Franklin, 9th and Chestnut Sts	3.50	5.00
Broadwood, Broad and Wood Sts	2.00	4.00
Colonial, 11th and Spruce Sts	2.50	3.50
Covington, 37th above Chestnut St	2.00	3.00
Drake, 1512 Spruce St	4.00	6.00
Lorraine, Broad St and Fairmount Ave	2.50	5.00
Majestic, Broad St. and Girard Ave	2.50	4.00
Normandie, 30th and Chestnut Sts	2.50	3.50
Pennsylvania, 30th and Chestnut Sts	2.50	4.00
Rittenhouse, Chestnut at 22nd St	2.00	3.50
Ritz Carlton, Broad and Walnut Sts	3.50	6.00
Robert Morris, 17th and Arch Sts	2.50	4.00
Roosevelt, 23rd and Walnut Sts	2.50	4.00
Spruce, 13th and Spruce Sts	2.00	3.00
St. James, 13th and Walnut Sts	2.50	4.00
Stephen Girard, 2027 Chestnut St	2.50	4.00
Sylvania, Juniper and Locust Sts	3.00	5.00
Walton, Broad and Locust Sts	2.50	4.00
Warwick, 17th and Locust Sts	4.00	6.00
Wellington, 19th and Walnut Sts	4.00	5.00

PRELIMINARY CLINICAL PROGRAM

GENERAL SURGERY GYNECOLOGY OBSTETRICS ORTHOPEDICS, UROLOGY NEUROSURGERY SURGICAL PATHOLOGY ETC.

JEFFERSON HOSPITAL

Monday

ROBERT P. PATTERSON—2. *The use of drugs in surgical cases*
WILLIS F. MANGUN—3. Treatment of acute infection by X-ray

Tuesday

VIRGIL H. MOORE—9. *Shock. Its mechanism, pathology and sequelle, illustrated.*
GEORGE A. ULRICH and staff—9. Obstetrical operations
DAVID M. DAVIS—9. Urological operations
ARTHUR FIRST—9.30. Sterility clinic.
J. TORRANCE RUTH—10. Orthopedic operations
P. BROOKE BLAND and staff—9. Obstetrical and gynecological operations.
CHARLES F. NASSAU—1. General surgery and ward walks
JAMES CARRELL—2. Ward walks
RANDALL MACCARROLL—12. Antenatal clinic
JOHN MONTGOMERY and CHARLES LINTON—12. Post operative follow-up clinic.
P. BROOKE BLAND and staff—3.30. Antenatal clinic, *demonstrations in laboratory clinical study of sterility* parasitic infestations of vagina
EDWARD J. KLOPP—2. General surgery

Wednesday

BROOKE M. ANSPACH, JOHN B. MONTGOMERY and staff—9. Gynecological operations
WARREN B. DAVIS—9. Plastic and oral surgery
HARRY STUCKEY and staff—9.30. Gynecological and obstetrical operations
P. BROOKE BLAND and staff—9. Obstetrical and gynecological operations
DAVID M. DAVIS—10. Urological operations, demonstration of cases
H. M. GREENBERG—10.30. Cystoscopic clinic
ARTHUR E. BULLADOR—1. General surgery and ward walks
EDWARD L. BAUER—12. Diagnosis and treatment of *pylorospasm and obstruction by congenital duodenal* bands, ward walk.
JOHN DUGGAR—12. Antenatal clinic
T. L. MONTGOMERY—12. Ward walks
P. BROOKE BLAND and staff—1.30. Antenatal clinic *demonstrations in laboratory clinical study of sterility* parasitic infestations of vagina
T. A. SHALLOW—2. General surgery
MARIO CASTALLO—2. *Treatment of carcinoma in* antenatal period, demonstration and presentation of cases.

Thursday

LEWIS C. SCHLEFFY, CHARLES LINTON and staff—9. Gynecological operations.
WARREN B. DAVIS—9. Plastic and oral surgery
T. L. MONTGOMERY and staff—9. Obstetrical and gynecological operations
P. BROOKE BLAND and staff—9. Obstetrical and gynecological operations.
DAVID M. DAVIS—10. Urological operations
HENRY K. SELLARS and P. A. MCCARTHY—1. General surgery and ward walks.
P. BROOKE BLAND and staff—1.30. Antenatal clinic, demonstrations in laboratory clinical study of sterility, parasitic infestations of vagina
E. J. KLOPP, W. F. MANGUN, F. C. KNOWLES, B. L. CRAWFORD and W. H. KEARNS—3. Tumor clinic conference
BROOKE M. ANSPACH and LEWIS C. SCHLEFFY—3. Clinical conference in gynecology
P. BROOKE BLAND—4. Obstetrical conference
T. L. MONTGOMERY and J. BERNARD BARNETTE—4. Manikin instruction

Friday

WARREN B. DAVIS—9. Plastic surgery operations.
GEORGE A. ULRICH and JAMES CARRELL—9. Obstetrical and gynecological operations
DAVID M. DAVIS—9. Urological operations
P. BROOKE BLAND and staff—. Obstetrical operations.
MICHAEL A. BURNS—10. Brain tumors
JOHN B. FLICK—1. General surgery and ward walks
LEWIS C. SCHLEFFY and W. J. TRUDEAU—. Uterine carcinoma, follow-up clinic
JACOB HOFFMAN—. Endocrinological clinic
JAMES CARRELL—2. Ward walks
JOHN DUGGAR—12. Antenatal clinic
ARTHUR FIRST and REGINA HORAN—3. Biological studies in pregnancy

HOSPITAL OF UNIVERSITY OF PENNSYLVANIA

Monday

Staff—2. Pre and postoperative care of surgical cases, demonstrations in the Laboratory of Surgical Research.

Tuesday

I. S. RAVDIN and *staff*—9. *General surgical operations.*
C. C. NORRIS and staff—9. Gynecological operations.
A. RANDALL—2. Urological operations
Staff—3. Demonstrations in the Laboratory of Surgical Research.

Wednesday

E. L. ELIASON and staff—9. General surgical operations.
C. C. NORRIS and C. BACHMA—9. Obstetrical clinic
Staff—. Pre- and postoperative care of surgical cases.
BRUCE GILL—3. Orthopedic clinic

Thursday

I. S. RAVDIN and staff—9. General surgical operations
I. E. KERNAN—9. Gynecological operations
BRUCE GILL—. *Orthopedic operations*
A. RANDALL—2. Urological operations

Friday

E. L. ELIASON and staff—9. General surgical operations.
Staff—9. Obstetrical clinic
C. C. NORRIS and staff—. Gynecological operations

EVANS INSTITUTE

Wednesday

R. H. IVY and LAURENCE CURTIS—10. Oral surgery

TEMPLE UNIVERSITY HOSPITAL

Monday

W EDWARD CHAMBERLAIN—1 Demonstration of biplane fluoroscope especially adapted for bronchoscopy
W EDWARD CHAMBERLAIN, CHARLES L BROWN, W EMORY BURNETT, CHEVALIER L JACKSON, LOUIS COHEN and ROBERT F RIDPATH—3 Chest conference
LAWRENCE W SMITH—3 Surgical pathological conference
W EDWARD CHAMBERLAIN and TEMPLE FAY—4 Hydrodynamics of the craniovertebral cavity, working model

Tuesday

W WAYNE BABCOCK—9 General surgical clinic.
TEMPLE FAY—9 Neurosurgical operations
JOHN FRICK—9 General surgical clinic
LOUIS COHEN—10 Artificial pneumothorax, ambulant cases.
J O ARNOLD—11 Intradermal test for pregnancy
JOHN O BOWER and staff—11 Surgical research laboratory
W EDWARD CHAMBERLAIN and TEMPLE FAY—11 Hydrodynamics of the craniovertebral cavity, working model
W EMORY BURNETT—1 Diseases of the breast
JOHN R. MOORE—2 Fractures, deliberate delayed reduction.
W HERSEY THOMAS—3 Genito-urinary clinic
FRANK W KONZELMANN—3 Surgical pathological conference
W EDWARD CHAMBERLAIN and TEMPLE FAY—4 Hydrodynamics of the craniovertebral cavity, working model

Wednesday

W WAYNE BABCOCK—9 General surgical clinic
J NORMAN COOMBS—9 General surgical clinic
TEMPLE FAY—9 Conference on neurological and neurosurgical problems, ward rounds
W EDWARD CHAMBERLAIN and TEMPLE FAY—11 Hydrodynamics of the craniovertebral cavity, working model.
W EMORY BURNETT—12 Plastic surgery clinic
W WAYNE BABCOCK and CHARLES L BROWN—1 Surgical medical conference
TEMPLE FAY—2 Fractures of skull and cerebral trauma
HARRY Z HIRSHMAN and staff—3 Proctological operations
LAWRENCE W SMITH—3 Surgical pathological conference.
W EDWARD CHAMBERLAIN and TEMPLE FAY—4 Hydrodynamics of the craniovertebral cavity, working model.

Thursday

W WAYNE BABCOCK—9 General surgical clinic.
JOHN LEEDOM—9 General surgical clinic
TEMPLE FAY—9 Neurosurgical operations, relief of pain
W EDWARD CHAMBERLAIN and TEMPLE FAY—11 Hydrodynamics of craniovertebral cavity, working model
JOHN O BOWER and staff—11 Surgical research laboratory
W EMORY BURNETT—12 Thoracic surgery clinic
TEMPLE FAY—1 Management of convulsive seizures, epilepsy
W EDWARD CHAMBERLAIN—1 Biplane fluoroscope especially adapted for bronchoscopy
J O ARNOLD—2 Toxemia clinic Demonstration of fluid balance, methods, case records and results
JOHN R MOORE—2 Orthopedic clinic Spine, angle point fusion, shoulder, posterior glenoid repair for luxation, hip, shelf procedure for shallow socket
W HERSEY THOMAS—3 Genito urinary clinic
FRANK W KONZELMANN—3 Surgical pathological conference
W EDWARD CHAMBERLAIN and TEMPLE FAY—4. Hydrodynamics of craniovertebral cavity, working model.

Friday

W WAYNE BABCOCK—9 General surgery
W EMORY BURNETT—9 General surgical clinic
TEMPLE FAY—9 Headache, its mechanism and methods of treatment
W EDWARD CHAMBERLAIN and TEMPLE FAY—11 Hydrodynamics of craniovertebral cavity, working model
JESSE O ARNOLD and staff—11 Obstetrical operations
JOHN O BOWER and staff—11 Surgical research laboratory
FRANK C HAMMOND—12 Gynecological clinic.
CHARLES L BROWN—1 Cardiac patients as surgical risks
TEMPLE FAY—2 Control of intracranial pressure by methods of dehydration
W EDWARD CHAMBERLAIN, CHARLES L BROWN, W EMORY BURNETT, CHEVALIER L JACKSON, LOUIS COHEN and ROBERT F RIDPATH—3 Chest conference
LAWRENCE W SMITH—3 Surgical pathological conference
W EDWARD CHAMBERLAIN and TEMPLE FAY—4. Hydrodynamics of craniovertebral cavity, working model

METHODIST EPISCOPAL HOSPITAL

Tuesday

CALVIN SMYTH and staff—9 General surgical operations
GEORGE J SCHWARTZ and staff—9 General surgical operations.

Wednesday

CALVIN SMYTH and staff—9 General surgical operations
GEORGE J SCHWARTZ and staff—9 General surgery
ROY W MOHLER—9 Cesarean section, Fothergill-Manchester operation for uterine prolapse
STERLING MOORHEAD—2 Urological operations

Thursday

ROY W MOHLER—10 30 Prenatal clinic.

ST MARY'S HOSPITAL

Tuesday

LEO WOJCZYNSKI—11 Uterine cancer

Wednesday

J M LAFERTY—9 Obstetrical clinic.
JOSEPH TOLAND—11 Pelvic infections, operative and nonoperative.

Thursday

WILLIAM F MORRISON—11 Perineal repair, including complete tears

CHILDREN'S HOSPITAL OF DREXEL HOME

Days to be announced

ALBERT C MARTIN Fluid balance in postoperative treatment
JOHN HAND Fractures in children.
J ALBRIGHT JONES Abdominal pain in children. Discussed by ELIZABETH KIRK ROSE.
J MONTGOMERY DEAVER. Appendicitis in childhood
GILSON C ENGEL. The treatment and results of hernia in children

ST JOSEPH'S HOSPITAL

Tuesday and Thursday

F HURST MAIER—10 The value of the Fothergill operation in the treatment of uterine prolapse.

PHILADELPHIA GENERAL HOSPITAL

Monday

H. R. Owen—1:30. General surgical operations.

Tuesday

William F. Moore—9. Treatment of bronchiectasis and pulmonary suppuration.
Henry S. Ruth and staff—9. Cyclopropane in thoracic surgery.
L. D. Engleheart—9. General surgical operations.
M. P. Warnock—9. General surgical operations.
C. A. Berkey—10. Treatment of gynecological cancer.
I. S. Hirschberg—11. Preparation of intravenous solutions and trays, demonstration.
Richard Meade—11. Management of pulmonary tuberculosis by means of artificial pneumothorax and allied operations.
Edward A. Schumann and staff—. Gynecological clinic.
Morris Bernstein—2. Thoracic surgery.

Wednesday

Henry S. Ruth and staff—9. Trends in anesthetic methods at Philadelphia General Hospital.
P. A. McCarthy and associates—9. General surgical operations.
John Bower and associates—9. Treatment of spreading peritonitis complicating acute perforative appendicitis, use of convalescent serum and peritoneal autotoxin.
I. S. Hirschberg—1. Preparation of intravenous solutions and trays, demonstration.
L. H. Clerf—1. Diagnosis and treatment procedures for intra-oral cancer.
W. G. Elmer and L. D. Fetterolf—3. Fractured hips.

Thursday

Temple Fay—9. Neurosurgery.
Henry S. Ruth and staff—9. Choice of anesthetic agents and methods.
L. D. Engleheart—9. General surgical operations.
M. P. Warnock—9. General surgical operations.
J. C. Howell—9. Breast cancer.
I. S. Hirschberg—11. Preparation of intravenous solutions and trays, demonstration.
Joseph MacFarland and staff—1. Tumor clinic—general discussion of management, treatment and diagnosis of various types of malignant diseases.
W. H. Machmoney—1. Urological operations, demonstration of cases.
John D. Reese—2. Plastic and oral surgery.

Friday

J. C. Howell—9. Cancer operations.
P. A. MacCarthy and associates—9. General surgical operations.
Henry S. Ruth and staff—9. Pre-anesthetic sedation.
I. S. Hirschberg—. Preparation of intravenous solutions and trays, demonstration.
B. P. Widmann—2. Technical procedures of X ray and radium therapy.

STETSON HOSPITAL

Wednesday

Stephen E. Tracy—9. Gynecological cases.

Friday

Stephen E. Tracy—9. Gynecological cases.

EPISCOPAL HOSPITAL

Tuesday

L. M. Boyer, J. W. Kloop and R. R. Layton—9. General surgery.
L. M. Boyer—12. Dry clinic: Amputations for diabetic gangrene.

Wednesday

H. E. Knox—9. Surgical management of pyloric and duodenal obstruction in infants.
R. H. Meade, Jr.—9. Factors influencing late results in treatment of acute perforation of peptic ulcers.
Lowry Allen—9. X-ray treatment of acute surgical infections.
E. T. Crossan—9. The management of acute osteomyelitis.
John Kloop and R. R. Layton—9. The management of fractures about the ankle.
Rutherford L. Jones—1. Orthopedic surgery.
Albert Martucci—4. The management of peripheral vascular disease.

Thursday

E. T. Crossan, H. E. Knox and R. H. Meade, Jr.—9. General surgery.

Friday

L. M. Boyer, J. W. Kloop and R. R. Layton—9. General surgery.

PRESBYTERIAN HOSPITAL

Tuesday

E. B. Hodge, E. L. Williamson and L. M. Rankin—9. General surgery.
R. H. Ivy and L. Curtis—9. Maxillofacial surgery.
A. B. Gill and T. E. Orr—1:30. Orthopedic surgery.
G. M. Laws, J. P. Lewis, D. Kimmel and J. F. Scholl—30. Gynecological operations.
C. Fouldrod, P. F. Williams, W. C. Ely, F. A. Miller and V. T. Shipley—4. Obstetrical conference.

Wednesday

William Bates, J. B. Marsh and J. C. Howell—9. General surgery.
J. C. Beardwood, F. A. Boyer and H. T. Kelly—10:30. Surgical aspects of diabetes, abdominal symptoms of diabetes, gangrene prophylaxis.
J. C. Bundell, F. G. Harrison, S. Earhart and Henry Sanders—1:30. Urology, operative and dry clinic.

Thursday

E. L. Eliason, F. A. Boyer and J. P. North—9. General surgery.
C. A. Berkey and J. C. Griffith—1:30. Gynecology.

Friday

H. P. Brown, Jr. and O. C. King—9. General surgery.
George M. Laws—1. Gynecology.

CHILDREN'S HOSPITAL

Days to be announced

W. E. Lee, Dr. Rosenau and O. King. General surgery.
Robert Ivy. Plastic surgery.
James Nicholson. Orthopedic surgery.

ST. VINCENT'S HOSPITAL

Wednesday

William F. Morrison—10. Gonorrhea of the female tract with complications.

GRADUATE HOSPITAL OF UNIVERSITY OF PENNSYLVANIA

Monday

JOSEPH C BIRDSALL, L T MILLIKEN, F G HARRISON and F ROSENBLUM—2 Genito urinary surgery, demonstration of cases

Tuesday

WILLIAM BATES—9 General surgery
WILLIAM H MACKINNEY and EDWARD A MULLEN—2 Genito-urinary surgery

Wednesday

WILLIAM R NICHOLSON—9 Gynecological surgery
WALTER ESTELL LEE and H L BOCKUS—9 General surgery

Thursday

FRANCIS C GRANT—9 Neurosurgery
JACOB W CUTLER—9 Intrapleural pneumolysis

Friday

ROBERT H IVY and LAURENCE CURTIS—9 Maxillofacial surgery
W E LEE and C T MARTIN—9 Lymphopathia venereum

PENNSYLVANIA HOSPITAL

Tuesday

NORRIS W VAUX—9 30 Gynecological and obstetrical operations, demonstration of cases and clinical exhibits
LEON HERMAN—2 Urological operations, demonstration of cases.

Wednesday

NORRIS W VAUX—9 30 Gynecological and obstetrical operations, demonstration of cases and clinical exhibits

Thursday

NORRIS W VAUX—9 30 Gynecological and obstetrical operations, demonstration of cases and clinical exhibits

Friday

NORRIS W VAUX—9 30 Gynecological and obstetrical operations, demonstration of cases and clinical exhibits.

NORTHEASTERN HOSPITAL

Tuesday

T T THOMAS—10 Fracture clinic - upper extremities

Wednesday

FREDERICK T KELLER and ALFRED H DIEBEL 2 Gynecological operations
T T THOMAS—10 Fracture clinic lower extremities
J B LOWNES and HAROLD LIPSHUTZ 2 Genito urinary clinic

Thursday

T T THOMAS—10 Fracture clinic upper extremities
FREDERICK T KELLER and ALFRED H DIEBEL Obstetrical clinic, demonstration of cases

Friday

T T THOMAS—10 Fracture clinic lower extremities

LANKENAU HOSPITAL

Monday

W H MACKINNEY—2 Urological operations

Tuesday

D B PFEIFFER J M DEAVER CLARK BROWN and EDWARD BORTZ—9 General surgery, operations and demonstration of cases

Wednesday

G P MULLER G C ENGEL, DR MAY and J KEEZEL—9 General surgery operations and demonstrations

Thursday

D B PFEIFFER, J M DEAVER, CLARK BROWN and EDWARD BORTZ—9 General surgery, operations and demonstration of cases

Friday

G P MULLER, G C ENGEL, DR MAY and J KEEZEL—9 General surgery, operations and demonstrations

WOMAN'S MEDICAL COLLEGE HOSPITAL

Tuesday

J S RODMAN and associates—11 General surgery

Thursday

LIDA STEWART COCILL and CONSTANCE WOLF—9 Postnatal clinic
HELEN M ANGELUCCI—9 Treatment of trichomonas vaginalis
FAITH FETTERMAN—10 Postirradiation lesions of urinary tract
LIDA STEWART COCILL—11 Ward walks with demonstration of interesting cases
MARGARET STURGIS and ELEANOR BALFE—11 Sterility clinic Tubal insufflation and lipiodol injections.
ANN GRAY TAYLOR—1 Prenatal clinic
CATHERINE MACFARLANE and FAITH FETTERMAN—2 Gynecological operations
CATHERINE MACFARLANE and VIRGINIA RIFFLEY—3 30 Treatment of dysfunctional uterine bleeding

ST AGNES HOSPITAL

Monday

W H HAINES—12 30 Genito urinary surgery

Tuesday

C C MURPHY—9 General surgery
J A McGLINN and W B HARER—9 Gynecology
H SANGMEISTER, W SUSSMAN and Y I YOSHIDA—9 Obstetrical clinic

Wednesday

J W BRANSFIELD—9 General surgery
G M DORRANCE—9 Plastic surgery
L WEFFT and W SUSSMAN—9 Gynecology
H SANGMEISTER W B HARER and Y I YOSHIDA—9 Obstetrical clinic
W H HAINES—2 Genito-urinary surgery

Thursday

A P KELLAN—9 General surgery
J A McGLINN—9 Gynecology
H SANGMEISTER, W B HARER W SUSSMAN and Y I YOSHIDA—9 Obstetrical clinic

Friday

G M DORRANCE and J W BRANSFIELD—9 General surgery
J A McGLINN and L WEFFT—9 Gynecology

AMERICAN ONCOLOGIC HOSPITAL

Tuesday

GEORGE M. DORRANCE—11 Conference on neoplastic diseases
GEORGE M. DORRANCE—3. Plastic surgery and surgery of malignancy

Wednesday

GEORGE M. DORRANCE—11 Conference on neoplastic diseases.

Thursday

STEPHEN E TRACY—9. Carcinoma of uterus.
GEORGE M. DORRANCE—1 Conference on neoplastic diseases.
GEORGE M. DORRANCE—3 Plastic surgery and surgery of malignancy

Friday

GEORGE M DORRANCE—11 Conference on neoplastic diseases

MOUNT SINAI HOSPITAL

Monday

M BERKELEY—1 15. General surgical operations

Tuesday

E L ELLIOTT—9 General surgical operations
B LIPPITTS—9 General surgical operations.
M MERCHAT—1 30 Urological operations.

Wednesday

C MAYER—9 Gynecological operations.
M COOPERMAN— Orthopedic surgery

Thursday

B MANN—9 Gynecological operations
M MERCHAT— 30 Urological surgery

Friday

B LIPPITTS—9 General surgical operations.
M BERKELEY—1 15 General surgery

GERMANTOWN HOSPITAL

Tuesday

E. B HOOGE, W B SWARTLEY S D WEEPER and R. S. ALSTON—10 30 General surgical clinic
Dr McLAUGHLIN and S S. WOOLSTON— 30 Varicose vein clinic

Wednesday

STANLEY Q WEST—9 Urological operations
C. F MITCHELL, W E LEE, H E KNOX and T M DOWNS —9 30 General surgical clinic
W E LEE and T M DOWNS— Thoracic surgery

WOMEN'S HOMEOPATHIC HOSPITAL

Tuesday and Friday

B F BRIGGS and I L HUGHES—9 Gynecology and obstetrics.

ST CHRISTOPHER'S HOSPITAL

Wednesday

HARRY E KNOX, JOHN WOLF and L M EALE Surgery of childhood

SHRINERS' HOSPITAL

Days to be announced

JOHN R MOORE. Orthopedic surgery

COOPER HOSPITAL
(Camden, N J)

Tuesday

B F BUDDY and Dr. CARLAVOTTE—9. Orthopedic operations.
T B LEE and G F WEST—9 Gynecological operations.
P M MEYERAY A S ROSS, F W SHAFER and I E DEMERRY—10. General surgery
R. S GAMON—10 Fracture clinic and demonstration of cases.
A B DAVIS, J HARRIS UNDERWOOD, LAWRENCE GLOVER and GEORGE B GERRAN—11 30. Prenatal clinic, demonstration of obstetrical cases.
A. H LIPPINCOTT, D F BENTLEY Jr and R R BEDINCOURT—1 Urology

Wednesday

P M MEYERAY A S ROSS, F W SHAFER and I E DEMERRY—9 General surgery
A B DAVIS and staff—9 Obstetrical clinic.

Thursday

B F BUDDY and Dr. CARLAVOTTE—8 Orthopedic operations
T B LEE and G F WEST—9 Gynecological operations.
P M MEYERAY and staff—10. General surgery
A B DAVIS, J HARRIS UNDERWOOD, LAWRENCE GLOVER and GEORGE B GERRAN—1 30 Prenatal clinic, demonstration of obstetrical cases
A B DAVIS— Obstetrical operations

Friday

Staff—9 General surgery operations and dry clinic

JEWISH HOSPITAL

Tuesday

J B LOWNES—9 Urological operations.
M BERKELEY—9 General surgery
W H TELLER—8. General surgery

Wednesday

F B BLOCK—9 General surgery
M BERKELEY—1 General surgery

Thursday

C J STARR—9 Gynecology and obstetrics.
F B BLOCK—1 General surgery

Friday

R GOLDSMITH—9 General surgery
F F WILLIAMS, C J STARR, J WALKER and F C HARRISON—9 Obstetrical and gynecological clinic.
W H TELLER—1 General surgery

BRYN MAWR HOSPITAL

Tuesday

A BILLINGS and staff—10 General surgery

Wednesday

W E LEE and staff—1 General surgery

Thursday

J S RODMAN and staff—10 General surgery
LEON HERMA —1 Urological operations.

KENSINGTON HOSPITAL

Days to be announced

A E PARKE, A D VOORHEES, J H MORRITT, Jr SAMUEL STEPP Z B NEWTON and F J KOWALSKI. Gynecological and obstetrical clinics.

MISERICORDIA HOSPITAL

Tuesday

B R. BELTRAN and E J GARVIN—9 General surgery, operative and dry clinic.
G P MULLER, F MOGAVERO and F T MCGINNIS—9 General surgery, operative and dry clinic.
J A SHARKEY—10 Planned obstetrical admissions and their influence upon obstetrical mortality and morbidity

Wednesday

J A KELLY and D C GEIST—9 General surgery, operative and dry clinic.
T J RYAN, J F DOUGHERTY and J B CLAFFEY—9 General surgery, operative and dry clinic.
F A. LOEFFLAD—10 Varicose vein clinic.
A KURTZ—11 Orthopedic clinic
W J MACMURTRIE—2 Toxemias of pregnancy

Thursday

G P MULLER, F MOGAVERO and F T MCGINNIS—9 General surgery, operative and dry clinic
B R BELTRAN and E J GARVIN—9 General surgery, operative and dry clinic.
J V MISSETT—2 Reduction of breast complications during puerperium

Friday

T J RYAN, J F DOUGHERTY and J B CLAFFEY—9 General surgery, operative and dry clinic
J A KELLY and D C GEIST—9 General surgery, operative and dry clinic
D C GEIST—10 Nerve lesions due to trauma
A E BOTHE—11 Tumors of the bladder

ST LUKE'S AND CHILDREN'S HOSPITAL

Tuesday

D ROMAN, R W LARER, H K ROESSLER and staff—9 Thyroid clinic, general surgical operations
E. A. TYLER—9 Anesthesia, demonstrations
WARREN C MERCER—9 Gynecological clinic.

Dry clinic—2

E. W ROBERTSON The heart and vascular system in relation to abdominal surgery with special reference to gall bladder surgery
D W KRAMER. Diseases in metabolism in relation to surgery
S L. IMMERMAN Recognition of postoperative pulmonary complications

Wednesday

L. AVERETT and staff—9 Obstetrical and gynecological operations
L. F MILLIKEN—9 Renal lithiasis in which renal sympathectomy has been done or might be done to prevent recurrence of stones

Thursday

A. W HAMMER, S HANDCOCK and E H DENCH—9 General surgical operations
WILLIAM C HUNSICKER, SR. and staff—9 Genito-urinary clinic.
WARREN C MERCER and staff—3 Obstetrical clinic.

Friday

J A BROOKE and staff—9 Orthopedic operations and demonstration of cases

CHESTNUT HILL HOSPITAL

Tuesday

FRANKLIN L PAYNE—9 Gynecological surgery
J F MCCLOSKEY, J A LEHMAN and J M ELIZEY—10 General surgery
ROBERT CADMAN—3 Allergy in surgical diagnosis
F K ALEXANDER—4 Demonstration of unusual X-ray films

Wednesday

WILLIAM B SWARTLEY, S DANA WEEDER and STEPHEN WOOLSTON—10 General surgery
EDWARD SCHUMAN and Z B NEWTON—10 30 Obstetrical operations

Thursday

WILLIAM C SHEEHAN, L H HERGESHEIMER and HANS MAY—10 15 General surgery
OWEN TOLAND, H C WOOD and W TOMPKINS—11 Obstetrical clinic and demonstration of cases
ALEXANDER RANDALL, FREDERICK SCHOFIELD and FRANK MASSINISO—2 Genito-urinary surgery
JOSEPHUS T ULLON, EDWARD MCCLOSKEY and FRANK M RAMSEY—3 Symposium on surgical failures

Friday

FRANCIS C GRANT—9 Neurosurgery
Staff—10 30 Presentation of cases showing interesting bone lesions in traumatic surgery
EDWARD F CORSON—1 30 Dermatological clinic, skin lesions in surgery

WOMAN'S HOSPITAL

Monday

ELEANOR BALPH—1 Urological clinic.

Tuesday

MARGARET STURGIS—9 Sterility clinic.
MARGARET STURGIS, ELEANOR BALPH and HELEN ANGELUCCI—10 Gynecological operations
DOROTHY CASE BLECHSCHMIDT—2 Breast clinic, demonstration of cases, X-ray films, follow-up studies, methods of diagnosis, discussion

Wednesday

MARGARET SUTLEY—9 General surgical operations.
ALBERTA PELTZ—10 Prenatal obstetrical clinic, toxemias of pregnancy, open discussion
LIDA STEWART COGILL—2 Obstetrical analgesia

Thursday

DOROTHY CASE BLECHSCHMIDT—9 General surgical operations

Daily Demonstrations

B M MEINE Pathological exhibit.
MARY EASBY Electrocardiological demonstrations, studies of its value in cases of surgical risk
DOROTHY CASE BLECHSCHMIDT—2 Motion pictures of abdominal surgery

ABINGTON HOSPITAL

Wednesday

ALEXANDER RANDALL—9 Urological operations
D B PFEIFFER, C SMYTHE, J W LEVERING, I BOYKIN, J M DEAVER, GEORGE M PIERSOL and DR EIMAN—2 General surgical clinic. Operations and demonstration of cases.

HAHNEMANN HOSPITAL

Tuesday

L. T. Armstrong, W. C. Hemmeter and staff—9. Operative clinic: Nephrotomy; prostatectomy; transurethral resection, Lusk-McCarthy punch, demonstration of sacrocaudal block; choice of anesthetics in urological surgery. Presentation of cases of renal pathology, pyelographic studies, vesical neoplasms, results of radiation and endocrinal therapy; presentation of cases, urograms and cystograms; a resumé of experimental studies in cortical representation of vesical function, illustrated demonstration of pathological specimens.

A. B. Wyatt—9. Fracture clinic.

Wednesday

H. L. Northrop—3. General surgery; motion picture demonstration.

Thursday

W. M. Sylvis—9. General surgery.
Thomas L. Doyle—9:30. Plastic surgery.
John Brooke— Orthopedic clinic.

Friday

G. A. VanLennep—9. General surgery.
J. M. Schofield—3. Diseases of the rectum.

Days to be announced

William Kiefer. Gastric pathology; demonstration of the Wolf-Schindler flexible gastroscope.

FITZGERALD-MERCY HOSPITAL

Tuesday

J. A. Kelly and T. J. Ryan—9. General surgery.
W. B. Harte—11. Gynecology.

Wednesday

B. R. Beilman and A. Burke—9. General surgery.
J. Mooney—11. Gynecology.

Thursday

J. A. Kelly and T. J. Ryan—9. General surgery.
J. McCarty—11. Gynecology.

Friday

B. R. Beilman and A. Burke—9. General surgery.
W. B. Harte—11. Gynecology.

FRANKFORD HOSPITAL

Tuesday

L. D. Eaglesiff—9. General surgery.
W. E. Parke—10:30. Gynecological operations.
George C. Hanna and associates—3. Obstetrical clinic.

Wednesday

W. E. Parke—9:30. Gynecological clinic.

Friday

L. D. Eaglesiff, R. H. Chandler and R. W. Lorry—9. Fracture demonstration.

SURGERY OF THE EYE, EAR, NOSE, AND THROAT

WILLS EYE HOSPITAL

Monday

FRANK C. PARKER—2 Operations.
THOMAS A. O'BRIEN—2 Dry clinic.

Tuesday

FRANCIS H ADLER—1 Operations

Wednesday

THOMAS A. O'BRIEN—2 Dry clinic
FRANK C PARKER—4 Operations

Thursday

F H ADLER—1 Operations

Friday

THOMAS A O'BRIEN—2 Operations
F C PARKER—2 30 Operations

Days to be announced

ALFRED COWAN Slit-lamp technique
MILTON J GRISCOM Unusual external diseases
EDMUND B SPAETH Plastic surgery of the eyelids
LEIGHTON F APPLEMAN Testing for phorias

MISERICORDIA HOSPITAL

Monday

J R. BRENNAN—2 Nasal hyperesthesia, treatment by zinc ionization

Wednesday

GABRIEL TUCKER—2 Bronchoscopic clinic

Thursday

C T MCCARTHY—2 Three cases of lateral sinus thrombosis with recovery

Friday

J A. LOFTUS—2 Mastoidectomy

FITZGERALD MERCY HOSPITAL

Monday

C T MCCARTHY—2 Otolaryngology

Tuesday

H. S BUSLER—2 Otolaryngology

Wednesday

J LOFTUS—2 Otolaryngology

Thursday

C. T MCCARTHY—2 Otolaryngology

Friday

H S BUSLER—2 Otolaryngology

WOMAN'S MEDICAL COLLEGE HOSPITAL

Wednesday

CHEVALIER JACKSON and EMILY L VAN LOON—9 Bronchoscopic clinic

GRADUATE HOSPITAL OF UNIVERSITY OF PENNSYLVANIA

Monday

GEORGE M COATES—2 Nose and throat surgery

Tuesday

RALPH BUTLER—2 Nose and throat surgery

Wednesday

GEORGE B WOOD—2 Nose and throat surgery
LUTHER C PETER—2 Ophthalmological surgery

Thursday

RALPH BUTLER—2 Nose and throat surgery

JEFFERSON HOSPITAL

Tuesday

H H LOTT—9 Nose and throat operations
CHARLES E G SHANNON—2 Eye operations

Wednesday

LOUIS H. CLERF—9 Bronchoscopic clinic.
AUSTIN T SMITH—10 Nose and throat operations.

Thursday

A J WAGERS—9 Nose and throat operations.
LOUIS H CLERF—12 30 Bronchoscopic clinic.

Friday

CHARLES E G SHANNON—3 Eye operations

ST LUKE'S AND CHILDREN'S HOSPITAL

Monday

J W POST and FRANK W BURGE—2 Clinical and X-ray study of bronchography

Wednesday

GEORGE MACKENZIE—2 Nose and throat operations
PHILIP S STOUT—2 Tonsillectomy by eversion method, modified radical mastoid

Thursday

S H BROWN, F C PETERS and staff—2 Ophthalmological operations

Friday

S A. BRUMM and staff—2 Nose and throat operations

PRESBYTERIAN HOSPITAL

Monday

G M COATES, W L CARISS and staff—1 30. Otolaryngology
H. M LANGDON, J THORINGTON and staff—3 Ophthalmological operations and demonstration of cases.

Wednesday

G M COATES, W L. CARISS and staff—1 30 Otolaryngology

HOSPITAL OF UNIVERSITY OF PENNSYLVANIA

Tuesday

GABRIEL TUCKER—9 Bronchoscopic clinic.
Staff—2 Nose and throat operations, demonstration of cases and conference

Thursday

Staff—2 Nose and throat demonstrations and conference.

Friday

GABRIEL TUCKER—2 Bronchoscopic clinic.

EPISCOPAL HOSPITAL

Monday

J A BERTOLET and staff—2 Nose throat and sinus surgery
ANDREW KNOX—4 Diseases of the eye
K A KASPER—4 Anatomy of the nasal accessory sinuses

Tuesday

N M BRINKERHOFF—2 Ophthalmological operations

Thursday

OTTO HIRST and staff—2. Nose throat and sinus surgery
N M BRINKERHOFF—2 Eye clinic

WOMAN'S HOSPITAL

Monday

EMILY L VANLOON—2. Bronchoscopy clinic Rôle of bronchoscopy in treatment of asthmatic cases, showing of X-ray films and case discussions
HENRIETTA TANNER—3 Ear nose and throat operations

Thursday

MARY BUCHANAN—2 Surgery of the eye, removal of cataract

HAHNEMANN HOSPITAL

Tuesday

H S WEAVER and staff—2 Otolaryngological clinic

Wednesday

H. S WEAVER and staff—2 Otolaryngological clinic

Thursday

H S WEAVER and staff—2 Otolaryngological clinic

CHILDREN'S HOSPITAL OF DREXEL HOME

Days to be announced

RALPH BUTLER Mastoids in children.
J A BARRITT The problems of the nose and throat in children

FRANKFORD HOSPITAL

Thursday

FRANK EMERY and associates—2. Ear nose and throat clinic

CHESTNUT HILL HOSPITAL

Tuesday

JOHN B DAVIES and GEORGE T PARIS—2 Otolaryngological operations

Wednesday

B. D PARKER and T TRAGANZA—2 Otolaryngological surgery

Thursday

CARL WILLIAMS—1 30 Ophthalmological surgery

Friday

CHEVALIER JACKSON—9 30. Bronchoscopy

ST AGNES HOSPITAL

Monday

G F J KELLY—4 Eye clinic

Tuesday

L. D SULLIVAN and A A S. GIORDANO—12 30 Nose and throat clinic.

Thursday

L D. SULLIVAN and A. A S GIORDANO—12 30. Nose and throat clinic

Friday

G. F J KELLY— 2 30 Eye clinic

JEWISH HOSPITAL

Monday

A BRAY—1 Ophthalmological clinic

Thursday

H M GODDARD—2 Submucous resection with nasal suction curette.

Friday

A BRAY— Ophthalmological clinic.

COOPER HOSPITAL
(Camden, N J)

Monday

J S BRIPMAN and staff— Eye surgery

Wednesday

O R KLINE, L. B HIRST and J P BRIPMAN—2 Nose and throat surgery

METHODIST EPISCOPAL HOSPITAL

Tuesday

WALTER ROBERTS and staff— Otolaryngological operations

CHILDREN'S HOSPITAL

Days to be announced

A PEWELL Ophthalmological surgery

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